

Europe Skeptical of Biometric Study of UGDP

Continued from page 1

imply structural weaknesses in the Bedford study in Britain were sharply rejected by Professor Harry Keen when he was contacted by MEDICAL TRIBUNE. Dr. Juhani Paasikivi, whose study in Sweden was briefly considered by the Biometric Society, noted that they had not contacted him beforehand. He maintained that his data favored the oral agents.

Dubious on Extrapolation

Clinicians in Britain, Belgium, Sweden, France, Germany, and Switzerland indicated that they continue to have doubts about the wisdom of extrapolating the findings of the U.G.D.P. study to bigger diabetic populations.

In certain situations, European physicians consider that the oral agents are an essential part of their armamentarium. However, their use of hypoglycemics is tinged with caution, and the overall tendency is to use much reduced dosages wherever possible.

"The possible risks must be weighed against the advantages, as in all drug therapy," said Dr. Bernard Rilliet, liaison officer with the World Health Organization for the International Diabetes Federation.

The data from the study by Dr. Robert Feldman and colleagues in San Francisco run up to late in 1974, covering a 10-year period. Despite the comparability of the research to the U.G.D.P. work, the Biometric Society did not ask Dr. Feldman for information, he said.

Expressing some surprise at this, Dr. Feldman, who is now working in Milan, Italy, said that of the 350 ambulatory patients who first entered the study, a total of 174 were given tolbutamide treatment. "So this is close to the size of the U.G.D.P. group," he pointed out. "This is an ongoing study, and I would have thought that the Biometric Society would want to take it into account."

Up to the end of last year, Dr. Feldman went on, there was no indication in his study of a rate of cardiovascular mortality comparable to that found by the U.G.D.P. There was a similar discrepancy in regard to non-fatal cardiovascular events.

Patients in his study were newly discovered asymptomatic diabetics, aged 15 to 59, and free of other disease. They were randomly assigned to tolbutamide (1 Gm. daily), phenformin (100 Mg. daily), or placebo.

A Younger, Healthier Group

A major difference from the U.G.D.P. study, Dr. Feldman commented, was his age-group, which was younger and healthier. "Their population was very old, and the disease was in many cases by then beyond any kind of prevention," he went on. "Furthermore, their statistics were skewed by the fact that they had no deaths attributable to myocardial infarction in the control group. This was such an unlikely outcome that it has to distort any attempt to match with a drug for comparability."

Like the U.G.D.P. researchers, Dr. Feldman's group did not begin with mortality as a target, but began to pay more attention to this parameter as a

result of the growing interest in the question. "Interestingly, of the seven myocardial infarctions to date, none have been associated with phenformin," said Dr. Feldman.

Of the Biometric Society's conclusions in general, Dr. Feldman said they left him with a feeling of scientific unease. "The U.G.D.P. study was a very noteworthy attempt to gather information in what is a very complex situation, what is lacking, however, is the total view. The net result is that we are left with the impression now that a lot of rather disparate pieces of evidence are being put together to support the arguments based on that one study."

Attempts by the Biometric Society's assessors to diminish the significance of the Bedford study on structural grounds were completely rejected by Professor Harry Keen at Guy's Hospital in London.

"Evidence emerged from our study that in regard to total arterial events at the five-year point, tolbutamide gave an advantage over placebo at a statistically significant level of 5 per cent," said Dr. Keen.

"But even though the material from our study was supplied to the Biometric Society at their request, they did not examine this claim. Instead, they suggested that our research was not properly randomized, and not double-blind. This I absolutely refuse to accept."

Telephone Directory Used

Dr. Keen said his team did not use a table of random numbers, but used the telephone directory instead. But this did not alter the fact that randomization was fully observed. The British method is one conventionally accepted by investigators.

Similarly, the code was broken only for ethical reasons (i.e. when considered essential for the patient's physician), and then only in five or six cases at most.

Discussing other aspects of the Biometric Society's criticisms, Dr. Keen said he and his colleagues in the study had never made a claim for tolbutamide specifically in regard to improved mortality. "If you look at mortality alone, you find that our findings do not contradict the U.G.D.P. study, but neither do they support them."

Dr. Keen, who with several other British investigators is helping to organize a 10-year prospective study on oral agents to be run by the British Medical Research Council, said that recently the Bedford findings were re-analyzed using a new life table method.

The new analysis has given no reason to change the previous conclusions favoring the use of tolbutamide, Dr. Keen said.

Discussing the attitude of clinicians in Britain, Dr. Alfred Bloom of the Diabetic Department, Whittington Hospital, London, said the accepted view is that oral agents are indicated when it is not possible to control the blood sugar in another way.

Dr. Bloom, who is a member of the executive council of the British Diabetes Association, and has done extensive research, said there are three alternatives for maturity-onset diabetics:

who do not respond to simple dietary restrictions:

- Leave them with the high blood sugar.
- Give insulin.
- Put them on tablets.

All three methods have obvious disadvantages, he continued, but these are most important in the first two approaches. To leave a patient of 50 or over with high blood sugar is unjustifiable, because of the increased risk of other clinical problems.

Dr. Bloom said there is much evidence that such patients have enough insulin. "If you give more, the result is to increase their body weight without reducing the blood sugar. So we don't feel this is indicated."

Oral hypoglycemics lower blood sugar, the tablets are easy and convenient for the patient, "and we give as low a dose as is necessary."

For One Kind of Patient

Dr. Bloom said he reserves the use of tablets for the kind of patient who does not respond to simple diet restrictions and does not need insulin.

"If the oral agents are used in this way, we see no reason in the light of the present evidence, to change our attitude concerning the value of this type of therapy," he concluded.

Although the study done by Dr. Juhani Paasikivi at Serafimer Hospital, Stockholm, is not exactly comparable to the U.G.D.P. study, he insisted that his findings are important and significant.

With a first infarction as the starting point, 178 patients were treated with tolbutamide as a therapeutic agent against placebo.

"Although, as the Biometric Society report points out, there was no significant difference in survival after two years, the point is that tolbutamide improved survival," said Dr. Paasikivi.

He noted that in the control group mortality was highest at the beginning of the two-year period, within the first six months after the infarction.

By comparison, those on tolbutamide showed better survival during this period, although mortality equalized over the longer segment.

Opposite of UGDP Finding

"Those who benefited most were those suffering from cardiac insufficiency and reduced glucose tolerance," Dr. Paasikivi observed. "This is the opposite of the U.G.D.P. findings, even though the groups are not quite comparable."

Dr. Paasikivi, who said he was surprised at not being approached directly by the Biometric Society, suggested that his group of patients was perhaps closer to those of Prof. Keen in Britain than to the overt diabetics of the U.G.D.P. study.

But he stressed that the findings contradict the U.G.D.P. conclusions, even though tolbutamide's effect in prolonging survival is not indefinite.

Professor Rolf Luft, of Karolinska Hospital, Stockholm, who is president of the International Diabetes Federation, said he is confirmed to recommend the oral drugs.

"I have not yet seen the Biometric

Suit Perils Free Clinic



Dr. Eugene Bathazar of Aurora, Ill., set up a free clinic when he "retired" after 45 years as a family doctor three years ago. Now he may have to close the clinic, which has treated 35,000 patients because one of them is suing him for \$100,000 for alleged malpractice and he carries only \$10,000 of insurance.

Society report, but I have given the U.G.D.P. study much attention, and was frankly not impressed," he told MEDICAL TRIBUNE.

Dr. Luft, said in his own clinical experience he has never encountered a patient death on the oral agents, and that he used mainly glibenclamide.

"I prescribe to patients with overt diabetes, who cannot be treated by diet alone—although we always try diet first—and we maintain close control and follow-up."

Asked if he had seen any sign of higher mortality rates in Sweden among diabetic patients, Prof. Luft said he was not aware of such a trend.

"I have had a number of discussions with my staff about this whole question of hypoglycemics, and we have come to the conclusion that they are valuable," he added.

[Next week: response from investigators in Belgium, France, West Germany, the U.S.S.R. and Switzerland.]

Sex Steroids Linked To Gum Inflammation

Medical Tribune Report

KANSAS CITY, MO.—An explanation for the gingival inflammation frequently observed in children at onset of puberty, in women on oral contraceptives, and during pregnancy has been put forward here by investigators at the University of Missouri School of Dentistry.

The probable cause, they said, is the increased concentration of sex steroids in blood and the augmented conversion of their inactive forms to active ones.

Incubation in vitro of 4-androstenedione and estrone with slices of inflamed human gum tissue found markedly enhanced the conversion of weakly active steroids into the most potent naturally occurring forms of both male and female sex hormones, testosterone and estradiol-17 beta, respectively, the investigators reported.

Gram-Negative Organisms Gain Resistance

By EDWARD GROSSMAN
Medical Tribune Staff

DENVER—Reviewing recent developments in bacterial infections and antibacterial therapy, Dr. T. Jacob John, Assistant Professor of Pediatrics, University of Arizona Medical Center, gave the American Academy of Pediatrics some bad news and some good news.

The bad news is that acquired antibiotic resistance among certain gram-negative organisms is on the increase, and can be expected to increase further. This resistance is mediated through so-called "R factors," Dr. John said, which are DNA molecules separate from the bacterial genome itself, present in some bacteria such as E. coli.

A unique property of these molecules is that bacteria possessing them pass them on to their neighbors, both those of the same and different species. Thus R factor-related resistance is infectious, and with the ever-growing use of antibiotics causing population pressure on E. coli, it is not surprising that transmission of resistance to Shigella and other organisms has already been proven and its consequences seen clinically.

The Shigellosis Problem

"Shigellosis in the U.S. is becoming a major problem," Dr. John said. The predominant U.S. strains of Shigella are S. sonnei and S. flexneri, and both strains are showing strong resistance to the former drug of choice, ampicillin. 82 per cent of Shigellae isolated in centers on the East Coast are ampicillin-resistant, and in the Mid-West, 66 per cent, Dr. John reported. Fortunately, the vast majority of these strains remain chloramphenicol-sensitive.

Ampicillin-resistance is also complicating treatment of Hemophilus influenzae Type B infections. Resistant strains have been recovered from life-threatening infections such as meningitis and sepsis. Fortunately again, the strains are chloramphenicol-sensitive. But antibiotic sensitivity testing in Hemophilus influenzae is now extremely important, Dr. John emphasized.

The Type B strains are rendered ampicillin-resistant by their production of penicillinase. Therefore disk sensitivity results should be confirmed by testing for production of penicillinase by means of the capillary tube technique of placing colonies in the presence of penicillin and determining within 30 minutes whether antibiotic destruction, with formation of acid components, has occurred.

The Good News

Turning to the good news, Dr. John summarized some diagnostic and therapeutic advances on several fronts:

- Echocardiography now offers an unprecedentedly accurate means for diagnosing and locating pericardial effusion. Vegetations as small as one or two mm. on the heart valves are detectable.
- The new Limulus test for determining endotoxin activity permits the rapid diagnosis of gram-negative endotoxin-producing bacterial meningitis. False-positive and false-negative results are rare, Dr. John said.
- Therapeutically, "it has become clear that metronidazole is an effective drug against obligate anaerobic bacilli, though not very effective against cocci," Dr. John reported. Metronidazole so far is licensed mainly for parasitic disease.

After sensitivity-testing, the choice is ampicillin alone if the strain is sensitive, and if resistant, chloramphenicol alone.

In every case, clinical course and therapeutic response should be closely monitored.

In the management of household contacts of patients with meningococcal disease, Dr. John continued, physicians also face new problems. Sulfonamides are the drugs of choice only when there is prior information that the strain is sulfanamide-sensitive. Otherwise, minocycline and rifampin have been relied on for prophylaxis. However, in 1974 a number of reports indicated that at least one-third, and sometimes as many as two-thirds, of those to whom the usual prophylactic doses of minocycline were administered, developed symptoms of pronounced vestibular dysfunction.

The Center for Disease Control now recommends only rifampin for chemoprophylaxis. Yet when rifampin is used alone, Dr. John pointed out, resistant strains are quick to emerge. He said that though rifampin is still favored, there may be times when the physician is faced with a real dilemma in choosing the best medication—if any—for protecting contacts of patients with meningococcal disease.

AAP's Recommendations

Dr. John noted that the Committee on Infectious Diseases of the A.A.P. had lately made the following recommendations on antibiotic therapy of severe Hemophilus influenzae infections:

- In those localities where ampicillin-resistant strains have been recorded, and before the patient can actually be tested for sensitivity, a combination of ampicillin and chloramphenicol should be used. In areas where such strains have not appeared, ampicillin alone should be used to begin.

- After sensitivity-testing, the choice is ampicillin alone if the strain is sensitive, and if resistant, chloramphenicol alone.
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- Trimethoprim-sulfamethoxazole, in general world-wide use for many years but licensed in the United States primarily for treatment of chronic urinary tract infections in patients over 12, is gaining acceptance for therapy of a variety of bacterial conditions, including pediatric. It was recently used in ten infants ranging in age from eight days to three months suffering from gram-negative meningitis, with "very encouraging results and no significant side effects," Dr. John said. "It would appear that trimethoprim-sulfamethoxazole is a good standby to use when more conventional antibiotic medication fails. It may also be useful in multiply-resistant Shigella and Salmonella infections."

Finally, Dr. John noted that tetracycline is being pushed out of the pediatric armamentarium as newer drugs take precedence. However, tetracycline is not yet completely retired as a pediatric antibiotic, being indicated in ophthalmic and rickettsial diseases, and trachoma.

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CLINICAL NEWS NOTE: "When seduction of the patient has been established unequivocally, we should encourage the lawyers to sue initially for rape, not malpractice." (Dr. William Masters, see page 1).

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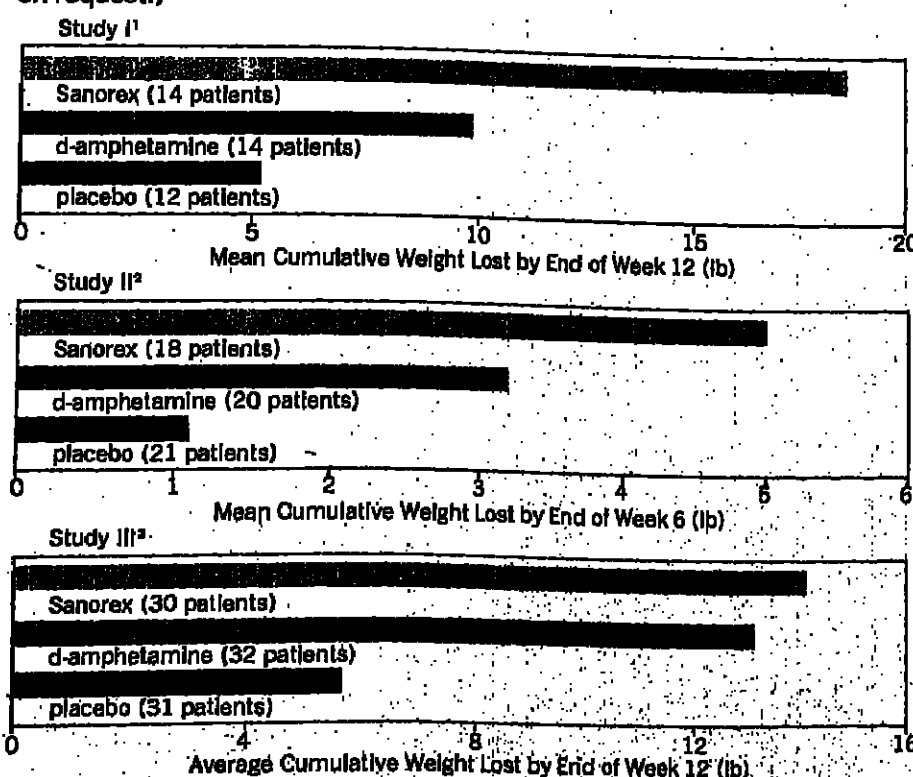
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*The significance of these differences for humans is uncertain.

For Brief Summary, please see facing page.

Wednesday, June 11, 1975

SANOREX[®] (MAZINDOL)[®]

References:
1. Kornhaber A: Problems and current concepts in the treatment of obesity. Scientific Exhibit presented at the New York State Academy of Family Physicians, 25th Annual Scientific Convention, Phylician, NY, May 8-10, 1973.
2. DeFolice EA, Cheykin LB, Cohen A: Double-blind clinical evaluation of mazindol, dextroamphetamine, and placebo in treatment of exogenous obesity. Curr Ther Res 15:358-366, July 1973.
3. Vernace BJ: Practical considerations for managing obese patients: Initial interview and effective treatment in the office. Scientific Exhibit presented at the American Medical Association, 27th Clinical Convention, Anaheim, Calif, Dec 1-4, 1973.

Indication: In exogenous obesity, as a short-term (a few weeks) adjunct in a weight-reduction regimen based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors.

Contraindications: Glaucoma; hypersensitivity or idiosyncrasy to the drug; agitated states; history of drug abuse; during, or within 14 days following, administration of monoamine oxidase inhibitors (hypertensive crisis may result).

Warnings: Tolerance to many anorectic drugs may develop within a few weeks; if this occurs, do not exceed recommended dose, but discontinue drug. May impair ability to engage in potentially hazardous activities, such as operating machinery or driving a motor vehicle, and patient should be cautioned accordingly.

Drug Interactions: May decrease the hypotensive effect of guanethidine; patients should be monitored accordingly. May markedly potentiate pressor effect of exogenous catecholamines; if a patient recently taking mazindol must be given pressor amine agents (e.g., levaterenol or isoproterenol) for shock (e.g., from a myocardial infarction), extreme care should be taken in monitoring blood pressure at frequent intervals and initiating pressor therapy with a low initial dose and careful titration.

Drug Dependence: Mazindol shares important pharmacologic properties with amphetamines and related stimulant drugs that have been extensively abused and can produce tolerance and severe psychologic dependence. Manifestations of chronic overdosage or withdrawal with mazindol have not been determined in humans. Abstinence effects have been observed in dogs after abrupt cessation for prolonged periods. There was some self-administration of the drug in monkeys; EEG studies and "liking" scores in human subjects yielded equivocal results. While the abuse potential of mazindol has not been further defined, possibility of dependence should be kept in mind when evaluating the desirability of including the drug in a weight-reduction program.

Use in Pregnancy: In rats and rabbits an increase in neonatal mortality and a possible increased incidence of rib anomalies in rats were observed at relatively high doses. Although these studies have not indicated important adverse effects, the use of mazindol in pregnancy or in women who may become pregnant requires that potential benefit be weighed against possible hazard to mother and infant.

Use in Children: Not recommended for use in children under 12 years of age.

Precautions: Insulin requirements in diabetes mellitus may be altered. Smallest amount of mazindol feasible should be prescribed or dispensed at one time to minimize possibility of overdosage. Use cautiously in hypertension, with monitoring of blood pressure; not recommended in severe hypertension or in symptomatic cardiovascular disease including arrhythmias.

Adverse Reactions: Most commonly, dry mouth, tachycardia, constipation, nervousness, and insomnia. Cardiovascular: Palpitation, tachycardia. Central Nervous System: Overstimulation, restlessness, dizziness, insomnia, dysphoria, tremor, headache, depression, drowsiness, weakness. Gastrointestinal: Dryness of mouth, unpleasant taste, diarrhea, constipation, nausea, other gastrointestinal disturbances. Skin: Rash, excessive sweating, clamminess. Endocrine: Impotence, changes in libido have rarely been observed. Eyes: Long-term treatment with high doses in dogs resulted in some corneal opacities, reversible on cessation of medication; no such effect has been observed in humans.

Dosage and Administration: 1 mg three times daily, one hour before meals, or 2 mg twice daily, one hour before lunch in a single dose.

How Supplied: Tablets, 1 mg and 2 mg, in packages of 100.

Before prescribing or administering, see package circular for Prescribing Information.

SANOREX PHARMACEUTICALS, EAST HANOVER, N.J. 07930

Current Opinion

What's In A Word? or Guilt By Definition—Part I

By DR. JONATHAN O. COLE

Psychiatrist, McLean Hospital, Belmont, Mass., and Lecturer in Psychiatry, Harvard University Medical School; excerpted from Massachusetts J. Mental Health, Winter, 1975.

I SUSPECT THAT throughout the history of mankind cosmic words or phrases have been used idiosyncratically by people in power, or wanting power, or by people with strong emotions or real or imagined fears to condemn the things they disapprove of. In my youth the term "communism" was used in that way to discredit any number of reasonable and sensible activities on the part of well-meaning people. Memories of the Joseph McCarthy era are still strong.

More recently, however, it has become possible to talk about communism in a much more meaningful and discerning manner. It has fortunately become manifestly clear that Russian communism and Chinese communism are very different... and a fair majority of the American people are able to contemplate communist regimes in various countries and consider the possibility that it might benefit the United States to have relations of some sort with a given communist country rather than rejecting the whole matter as being a sin and a crime.

I am now grieved and upset to see other terms... take on a similar monolithic connotation of evil.

Both "behavior modification" and "psychotropic drugs" are frequently referred to in newspaper articles and in scientific and political essays as being great evils which must never be imposed upon anybody. I believe this to be unmitigated obfuscating twaddle...

Both "behavior modification" and "psychotropic drugs" are frequently referred to in newspaper articles and in scientific and political essays as being great evils which must never be imposed upon anybody. I believe this to be unmitigated obfuscating twaddle... There is nothing inherently bad about either behavior modification or about psychotropic drugs.

Let's take behavior modification first. The term "behavior modification" in the literal sense simply means the changing of behavior. This is something that parents try to do to children from the time they are born until they leave home, something that religions have tried to do to human beings from time immemorial, and something legislatures pass laws to attempt to do with respect to citizens in general. In primitive tribes a wide variety of customs and taboos are developed for precisely this purpose. Obviously, society and social intercourse would deteriorate into total anarchy if some kinds of behavior modification and control did not exist.

A rose by any other name should smell just as sweet. Unfortunately, if you call a certain set of procedures "education," that's good, but if you call them "behavior modification," that's terrible. This is, patently ridiculous.

Teachers have for generations awarded gold and silver stars to children who did reasonably well...

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DR. JONATHAN O. COLE

behavior modification programs in prisons; I therefore cannot speak from experience and I agree in advance that there may have been unfortunate, unpleasant or even dangerous programs developed in prisons which have been called behavior modification.

Problem of Bad Programs

The fact that bad programs or even evil programs have existed does not make the concept bad—it means that a specific example of it was bad. Therefore, the recent statement by the head of the Law Enforcement Assistant Act (LEAA) that ALL behavior modification programs supported by that agency had been stopped struck me as a horror. Bad programs or harmful programs of any kind should be stopped when there is sufficient reason.

If LEAA had not been able to fund a single good program of behavior

"...therapeutic communities are not usually condemned for 'modifying behavior,' while behavior modification in prisons have been widely attacked..."

modification in prison, then its administrators and its grantees must be incredibly stupid, because the point at which rehabilitation programs stop and behavior modification programs begin must be extremely foggy and difficult to define. I suspect that good rehabilitation programs are called rehabilitation and bad ones are called behavior modification, even as good brain surgery is called brain surgery and brain surgery of which you disapprove is called psychosurgery.

This using of terms as epithets rather than as definitions is exactly the phenomenon to which I am most opposed.

Comparison With Life

Behavior modification programs, like life, contain one or more systems of reward or punishment which are aimed at suppressing, reducing, or eliminating behavior which is harmful to the individual or society and at encouraging, reinforcing, or increasing behavior which is beneficial to the individual or society. The usual difference between behavior modification programs and other types of social influence is that behavior modification programs are thought through in a good

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Minoxidil Shown Safe and Effective In Moderate-Severe Hypertension

By HARRIET PAGE
Medical Tribune Staff

SAN FRANCISCO—A new antihypertensive agent, minoxidil, has been shown to be a safe and effective treatment for moderate to severe hypertension, in double-blind crossover studies performed at the University of Michigan Medical Center. In 11 patients, said Dr. R. Kent Bryan, the drug decreased average supine blood pressure from 177/109 mm. Hg to 147/87 mm. Hg without serious side effects.

Reporting here at the annual meeting of the American College of Physicians, Dr. Bryan said the agent, which has investigational new drug status, had earlier been used only in critically ill hypertensive patients. He said he believes this is the first double-blind study in moderately ill patients.

'Nonspecific' ECG Changes

Dr. Bryan, a nephrology fellow, said the new drug caused no hematopoietic, gastrointestinal, or renal toxicity. It did cause "nonspecific" electrocardiographic changes, he said, but the significance of these is uncertain. It also caused weight increase, edema, and hirsutism.

The average weight gain over the six- to eight-week test period was 3.3 Kgs., Dr. Bryan said, but weight loss followed promptly after the drug was discontinued. Peripheral edema occurred in four of the 11 patients and was serious in two. He told MEDICAL TRIBUNE he believes this could be controlled by using a stronger diuretic than the one entered in the experimental protocol.

Hirsutism, which was most noticeable around the face, arms, and back, occurred in eight of the patients. "The ladies didn't like it," Dr. Bryan said, and it constituted a "serious complaint" in three of four of them. The fourth, Dr. Bryan said, had suffered from refractory high blood pressure for a number of years, "and preferred the hirsutism."

12 Patients Entered in Study

Twelve patients—eight men and four women—were originally entered in the study, but one, who suffered a hypertensive crisis while on placebo, was removed. Their average age was 52, and they had been receiving antihypertensive therapy for an average of 7.6 years. The average pressure before any therapy was 217/131 mm. Hg. They had suffered a number of hypertensive complications, including cerebrovascular accidents, congestive heart failure, left ventricular hypertrophy, and cardiomegaly.

The study consisted of three periods. During the control period, all the patients were given propranolol, 160 mg./day, and hydrochlorothiazide, 100 mg./day, and these were continued throughout the study. After approximately four weeks, when the supine diastolic pressure was stabilized between 100 and 120 mm. Hg, pre-randomized, coded tablets of minoxidil or placebo were added to the regimen. The drug was increased by 5 mg. increments every three days until the supine diastolic pressure was less than

90 mm. Hg or until a maximum dose of 40 mg./day was reached. Then the drug and placebo were switched until similar end points were reached. The last two periods consisted of approximately six to eight weeks each, Dr. Bryan said.

The average effective daily dose was 26.4 mg., Dr. Bryan said, and the maximal fall in blood pressure occurred within 24 to 48 hours after an increase in dose. He added that the study is expected to continue until July and will include a total of 20 patients.

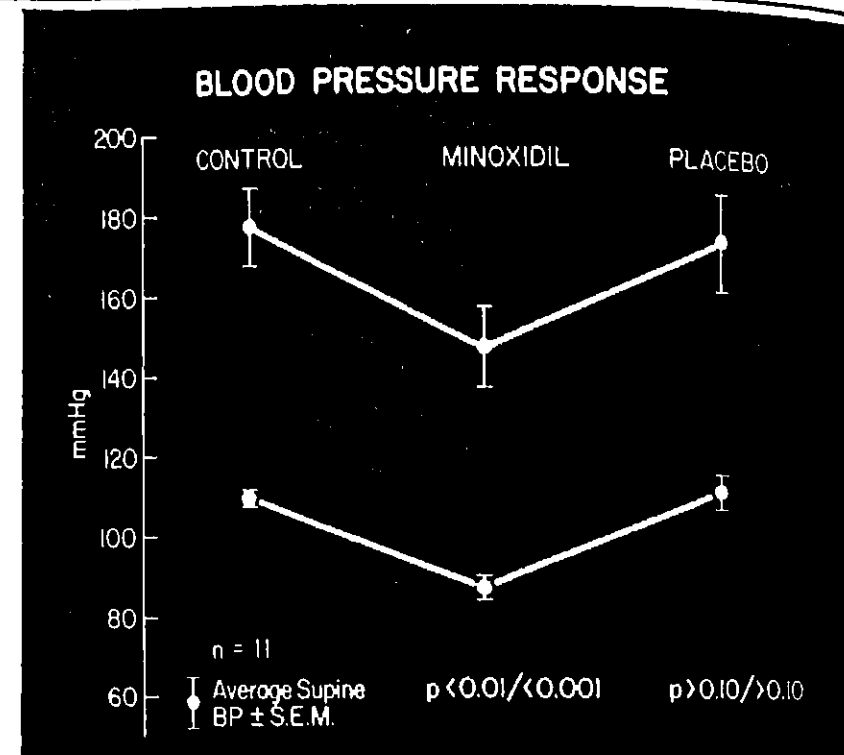
His coauthors were Dr. Jonathan Rosenzweig, Assistant Professor of Nephrology, and Dr. Sibley W. Hoobler, Chief of the Department of Nephrology.

Postpartum Hypertension

A transient, low-renin, postpartum hypertension appears to occur in about 9 per cent of young black women, according to investigators at Emory University School of Medicine.

Dr. W. Dallas Hall said the condition lasts for about six weeks, and occurs in mothers who are "slightly older and clearly heavier" than normotensive women in the same setting. He said he and his associates found the hypertension—which they set at pressures greater than 140 mm. Hg systolic and 90 mm. Hg diastolic—in 36 of 391 women whom they studied.

The mean blood pressure they found was 158/103 mm. Hg. "The entire



Systolic pressures (upper line) and diastolic pressures in 11 patients after stabilization on control drugs, minoxidil treatment, and after placebo period.

study population was very young, with a mean age of 21 years," Dr. Hall said. "Hypertensive patients, however, were about two years older, had more previous pregnancies, and were remarkably heavier. One third of the hypertensive group had toxemia in the preceding pregnancy, the remainder demonstrating de novo hypertension."

Mean plasma renin activity was found to be 0.22 ng./ml./hr. in the postpartum hypertensive patients, Dr. Hall said, compared with 1.24 ng./ml./hr. in the normotensive postpartum patients. Add in 16 young hyper-

tensive women who were not postpartum, Dr. Hall said, the mean plasma renin value was 1.47 ng./ml./hr.

The plasma renin activity was measured serially for 11 months in 11 of the postpartum hypertensive patients and was found to rise spontaneously in seven, though it remained low in four patients. The rise was usually apparent by three months postpartum when the blood pressure had returned to normal, he noted.

Coauthors were Margaret Douglas, Dr. James O. Wells, and George H. Worm.

Prazosin Successful in Hypertension Trials

By PATRICIA MCBROOM
Special Tribune Correspondent

PHILADELPHIA—A major new antihypertensive drug, prazosin, has proved successful in clinical trials, according to Dr. Gaddo Onesti of Hahnemann Medical College.

Dr. Onesti said he expects prazosin, already in use in England, to be licensed soon by the Food and Drug Administration.

In a report to the 169th annual meeting of the American Chemical Society here, Dr. Onesti said he has tested prazosin for about two years in some 60 patients and that the drug has advantages over other agents.

It is a peripheral vasodilator, but unlike other drugs of this class, it does not appear to cause reflex tachycardia, he said.

Seems to Lack CNS Effects

Also, because the drug acts peripherally, it seems to lack the sedative and other central nervous system effects of many antihypertensives now in use.

"Dr. Onesti expects prazosin to be useful in moderate to severe hypertension. 'For those patients who shouldn't have CNS interference, this drug will be ideal.' But for many patients, the tranquilizing effects of current drugs that block sympathetic nervous system activity may be desirable, he added.

"Enormous numbers of people are grateful for the sedation," he said. "You take their drug away and they feel tense all the time."

The complete pharmacology of the drug, Dr. Onesti said, is still unknown. "Prazosin must be doing something we don't understand. Whatever it is, it's good."

He speculated that the drug might have some limited central effects, since in one animal experiment, high doses of prazosin caused sedation.

Dr. Onesti, who is using the drug in patients with up to 130 mm. diastolic hypertension, said its potency lies somewhere between that of methyl dopa and clonidine, the latter being more potent.

He adds a diuretic to magnify the

antihypertensive effect. On rare occasions, he said, this has caused orthostatic hypotension.

Commenting on minoxidil, another experimental vasodilator, he said:

"Minoxidil is an extremely powerful drug and long acting," but its usefulness may be limited by the marked hirsutism accompanying its use, which many find objectionable.

Other members of the symposium on hypertension at which Dr. Onesti spoke said they foresee new drugs that will block sympathetic activity at both the vascular and cardiac levels, with minimum if any effects on the brain.



What Price Pure Science?—a 2-Sided Issue

By FRANCES GOODNIGHT
Medical Tribune Staff

ATLANTIC CITY, N. J.—"How do we go about proving that scientific knowledge at a genuinely basic level is essential for the conclusive solution of disease problems?"

Dr. Lewis Thomas, president of the Memorial Sloan-Kettering Cancer Center and author of the award-winning *Lives of a Cell*, raised this question here as he urged fellow scientists to face the fact that today's argument about the value of science is not a one-sided affair.

It is a genuine argument with two intelligible points of view, Dr. Thomas declared, and "the way it comes out may well determine the course of both biomedical science and the practice of medicine for the rest of this century and beyond."

Other Side of Argument

Investigators have had so strong a preference for "our side" of the matter that they tend to ignore major issues of disagreement, Dr. Thomas told a symposium at the annual meeting of the Federation of American Societies for Experimental Biology.

Members of the scientific camp, he noted, believe as an article of faith that biomedical science is an obvious good—worth whatever the cost.

On the other side are people who must make difficult, long-range decisions about allocations of money from a diminishing source of funds, he pointed out. They have a "practical conviction" that whenever substantial public funds are committed to an enterprise there should be hard evidence that the public will receive value for the money.

As Dr. Thomas sees it, demands made by "our side" for continuing and increasing support for biomedical science have aroused both skepticism and unease. Research costs more and more money and furthermore not all the benefits promised—"tacitly or explicitly"—over the past 20 years have materialized.

Solutions offered by science appear in the public view to be enormously expensive items of technology that aren't always the practical, conclusive measures society expected, he continued. Cancer is still present, as are heart disease and stroke plus a host of other major diseases—"and nobody makes house calls."

Science Before Technology

"It is our position that you need the science before you can devise the technology, and we argue that biomedical science is bringing in the kinds of information essential for the task," Dr. Thomas said. "We have, in our view, good examples of this all over the place."

But he warned that the case for fundamental science has not been stated convincingly enough. Since most people consider research "a sort of luxury, an intellectual indulgence," the argument that it is essential will have little success "unless we provide hard facts to go with the assertion."

What facts? Dr. Thomas thinks

there is solid evidence in the contribution made by biomedical research to the control of infectious disease—a field where biomedical science was so successful that "medicine was transformed from one kind of profession into another within a period of just a few years."

Yet this evidence has not been played up sufficiently in the running argument over the value of research, he added, because even those physicians who were around when the big change took place in medicine tend to forget about the science responsible for it.

Referring to personal experience, Dr. Thomas noted that he was an intern in 1937 when the sulfonamides arrived and saw the pattern of disease

change drastically in one big city hospital from that time on.

"But the control of bacterial infection did not begin in 1937 with the introduction of sulfonamides nor later with penicillin," he said. "It did not have its origin in Fleming's earlier discovery nor in Domag's still earlier work. It really began, rather ambiguously, around 1875. The indispensable science was microbiology itself and the subsequent progeny of this new science—immunology and virology."

Hard to Cut Corners

Massive research was necessary to establish that particular bacteria were responsible for particular diseases," Dr. Thomas said. And before the discipline of infectious disease could emerge

as a recognizable field of medicine, there had to be "over 50 years of the most painstaking, difficult, and imaginative basic science."

Doing it all over again today would require much the same sets of experiments, he continued. While the work might go more quickly, it would not be possible to "cut any corners or omit much in the way of detail."

Although Dr. Thomas stressed that much still has to be learned about bacteria, let alone viruses, he is convinced that investigators have demonstrated a measure of competence—based on science—in this one field of medicine.

When questions are asked about competence in other areas, he suggests that the answer should be that biomedical science has to be viewed as a "very young science," an investment or knowledge bank for the future.

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*See literature for details. © 1975, THE FORDS PRODUCE COMPANY/ATLANTA, GA 30303

if you've got money questions ...Eliot Janeway has the answers

Do you see any prospect of the government taking over the financing of college education? I have four children and three will be in college at once, and I'll be in the poorhouse. Isn't tax relief possible?

Father M.D.
None. Better be braced to see the government start reaching for new tax dollars from "the rich" to justify the spending spree it's on. You'd better start conditioning your college-age youngsters to work their way through college if they mean business about starting, much less finishing. Don't count on state institutions to stay cheap for very long, either.

Can we expect an upturn by fall? If so, what will be the factors that will bring it about?

Dr. Frederick W., New York
Not if the government continues to sit around and wait for it. But if Ford begins to act like a President and overrules Kissinger's veto or a confrontation, an upturn would follow within weeks after U.S. political initiatives knock the price of oil down.

I notice the Arabian oil producers are buying into oil-using industries—aircraft, automobiles. How do you explain that? Aren't their own high oil prices ruining those industries?

Model T. Doc
You've got it absolutely right. The explanation is simpler than you think: the petroprofits are dumber than you think, though not so dumb as to be puzzled because we're continuing to take it and like it.

Before the end of the year, I have to make a decision about my Keogh funds. I am thinking about a mutual fund. I am in my early fifties and will have about \$6,500 to invest. Any advice or suggestions would be appreciated.

G. A., M.D. Louisiana
I think Keogh funds are suitable for investors in your circumstances. However, my suggestion as to selectivity is that you choose income funds whose dividends you can compound rather than funds oriented toward growth and therefore involving speculation in volatile stocks while limiting income returns.

Is stock in these computerized telephone control systems a good buy?

Dr. Edward M. B., Iowa
No stocks will be good buys until long term interest rates are brought back down to 6%.

Is this a good time to replace office equipment, in your opinion? I can't imagine prices going down.

Dr. Ralph M., Omaha, Neb.
I see industrial prices going down, and therefore advise waiting until the stoppage now spreading throughout the economy offers bargains to cash buyers. It won't be long.

I have a large home with an open-end mortgage at 5½%, which is three-quarters paid off. Should I pay off the mortgage with some savings and then put what I am now putting into monthly mortgage payments into blue chip stocks which seem extraordinarily low to me? Seems to me I'd be ahead in the long run.

The Long-runner M.D.
Not even this government would be dumb enough to pay off a 5½% mortgage! It's worth its weight in gold (if gold were worth what it's cracked up to be). Blue chip stocks may seem low to you, but they're going considerably lower.

Do you have any advice for those of us small-town fellows who bought mutual funds?

Dr. M. M., Maine
If they're well managed, stick with them and buy more for the long pull. That's the only way mutual funds ever pay off, and they do for those with the means and the patience to continue accumulating them on the way down.

The fund managements which pass muster never put on a flashy performance in any year of speculative exuberance, but were always content to run a comfortable second. If it's any comfort to you, the well managed funds have always continued to grow through bad markets.

each week in
Medical Tribune

In addition to writing his evaluations of current economic trends, Eliot Janeway, a leading economic authority, regularly answers the questions of physicians about financial, real estate, stock and bond, tax and insurance problems.

If you have a question, send it to Eliot Janeway, c/o Medical Tribune, 880 Third Avenue, New York, NY 10022.

Wednesday, June 11, 1975

MEDICAL TRIBUNE

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Truly Scientific Clinical Trial Deemed Virtually Impossible

Medical Tribune World Service

DAVOS, SWITZERLAND—Though physicians pay homage to the "scientific method," a symposium on the Limits of Medicine was told here, it is almost impossible to construct a truly "scientific" study involving human subjects.

For one thing, said Dr. Gerhard Kienle, of the Herdecke Cooperative Hospital in West Germany, a statistical concept such as the normal distribution curve has little value when applied to biologic processes. "Nor is it possible," he added, "to establish the danger or the safety of a medical product for a human patient on the basis of animal studies."

For example, Dr. Kienle told the symposium, which was organized by the Gottlieb Duttweiler Institute here, it can't be proved clinically that a drug such as thalidomide is harmful to the fetus. "We can only infer this," he declared, "on the basis of disturbances in epidemiologic patterns and on an accumulation of direct medical observations."

At the ethical and methodologic levels, Dr. Kienle continued, there are major weaknesses in the concept of the controlled clinical test. He stated the ethical paradox as follows:

1. It is unethical to use a therapy whose effectiveness has not been demonstrated.
2. It is also unethical to seek to demonstrate the effectiveness of a therapy by scientific methods.

Conflict of Needs

One consequence, he commented, is that as soon as evidence begins to appear that a new therapy can either cure, alleviate, or protect against a disease, the individual need of the patient in the control group begins to compete with the technical requirements of the trial protocol.

Projections from a small pilot study may be so promising that the investigator conducting a major study would be forced to compromise the health, or even the life expectancy, of his controls if he wished to maintain the numbers required for complete randomization, Dr. Kienle said. The reality in such circumstances, he said, is that a double-blind study not only rules out the placebo effect, but also prevents the participating physicians from exercising their ethical judgment.

Apart from the ethical problems, Dr. Kienle went on, it is hardly possible to find a controlled clinical trial worthy of the name that is methodologically unassailable. He gave these examples:

- It has been shown in German studies that on occasion a particularly alert practitioner is already aware of the value of the substance under test, and manipulates the situation so that a pa-

tient who he thinks needs the drug is placed in the appropriate group.

• There is usually a huge discrepancy between the planned size of a study and the actual numbers that take part to the end. The duration required by scientific criteria may also prove impractical. A clofibrate study was intended to follow 2,000 patients, but reached only 500. An oral contraceptive study went on so long that when it ended the pill was no longer on sale.

"Any doctor who insists that without a controlled clinical study it is not possible to know whether a medication is effective, should give up the practice of medicine," Dr. Kienle advised.

Free Clinic Emphasizes Preventive Medicine



Most clinics concentrate on treating existing problems but a free clinic operated by black medical students at the State University of New York at Buffalo emphasizes preventive medicine. The Inner City Well Health Center provides a place where the healthy can get complete physical examinations. Above, medical student Gregory Morton checks a patient's ear.

Natural distinction

Wholesome and unadorned young beauty impresses the eye with its natural distinction. Among medicinals, such natural distinction will be found in SENOKOT Tablets/Granules.

Standardized senna concentrate has two claims to natural distinction. In SENOKOT Tablets/Granules, it is standardized for uniform action. And it is prepared from the de-seeded pod of *Cassia acutifolia*, discarding the leaves that contain coarctate resins.

Virtually colon-specific, SENOKOT Tablets/Granules provide gentle, predictable overnight laxation... usually without side effects at recommended dosage levels. As regular elimination is established, dosage can be reduced gradually and eventually discontinued.

Purdue Frederick

Senokot

Tablet/Granule
and vegetable laxative

Stooped Posture in Japan

Medical Tribune World Service

TOKYO—Many Japanese women over 30 have a stoop, according to a survey of 1,800 persons by Dr. Yoshitomi Yamaguchi, of Toho University. In men, this postural defect does not become common until the 50s, he said.

US Support of Health Research Abroad Shifts to Bilateral Basis

By ALAN FITZGIBBON
Special Tribune Correspondent

WASHINGTON—Collaboration in health research between the United States and other countries is slowly changing character and broadening in scope.

Until the late 1960s most U.S. Government interest in health matters abroad took two forms—participation in the work of such international bodies as the World Health Organization and its affiliates or financial support of foreign investigators, some of whom worked with colleagues in the United States.

In recent years the nature of official American interest in W.H.O.'s work has changed, the once-sizeable program of grants to investigators abroad has declined, and increased stress has been put on collaboration in health research with individual foreign countries in what are commonly called bilateral programs.

"We used to think of W.H.O. as purely a technical assistance organization which organized, supported, and often directed specific health projects in underdeveloped countries," said a Department of Health, Education, and Welfare official concerned with international health matters.

Dominated by Economists

"During the 1940s, '50s, and '60s we supported W.H.O. heavily and to some extent bankrolled health projects in the underdeveloped countries directly through the Agency for International Development and its predecessors. But by and large our thinking about investment in health projects abroad was dominated by the economists, and they gave health a low priority because there was no proof that it promoted economic development.

"We really weren't getting the results we hoped for in the health area, and, in addition, foreign aid that emphasized technical assistance came to be looked on as a drain on American resources. The heavy expenditures on the war in Vietnam and our increasingly unfavorable balance of payments resulted in growing restrictions on what we could spend abroad, so we began changing course."

For W.H.O. and related agencies, this meant increased American pressure to keep budgets down and later a cut in U.S. Government contribution from 33 to 25 per cent of these budgets. It also meant less American interest in specific health projects—development of a medical school here, of a potable water system there—and greater interest in W.H.O. programs to promote the development of basic health services and health infrastructures.

Dozens of Projects Halted

For hundreds of individual investigators abroad, the changed course meant a major curtailment of grants in aid and the halting of dozens of research projects. It also resulted in the closing of National Institutes of Health offices in London, Paris, Tokyo, and Rio de Janeiro that had provided liaison between foreign researchers and their sponsoring institutes in Bethesda, Md.

Critics of this shift both here and abroad say that much of the abandoned research was of high quality and should have gone on, but H.E.W. officials argue that most of what was given up was a luxury since it did not bear on immediate health problems in the United

States. H.E.W. is still spending about \$20,000,000 every year, however, on grants to individual foreign investigators.

Official American interest in "bilateral" programs, which began in 1961, increased greatly during the early years of the Nixon Administration, and there are now between 15 and 20, but defining them is no easy task.

Some H.E.W. officials stress their country-to-country nature, in opposition to the "multilaterality" of W.H.O. Others say in addition that "there is now American input, and people here really work with people there; we don't just give grants and ask for occasional progress reports any more."

The bases of the programs range from formal ministerial agreements detailing the work the United States and another country are to do (such as that between this country and the Soviet Union) to unwritten understandings that the United States and another country have mutual research interests. Some of the programs are large and involve dozens of regular exchanges between investigators here and abroad, such as the U.S.-U.S.S.R. cancer program, and others seem to consist largely of research news mailed between an American investigator and his colleague abroad.

Varied Financing Role

Sometimes the U.S. Government finances a research project in another country, sometimes it finances only the American portion of a collaborative project, and sometimes it finances nothing at all.

Bilateral programs began in a small way 14 years ago when Congress passed the now-famous Public Law 480, under which surpluses of a foreign currency that accumulated from U.S. agricultural sales could be used for worthy purposes in the country to which the sales had been made. For several years the only agencies interested in applying for and using Congress' annual appropriations of PL 480 funds were the Departments of Agriculture and of Health, Education, and Welfare, but more recently the Department of the Interior and of Transportation, the National Science Foundation, and other agencies have been making use of the funds.

Health programs were originally started in 11 countries where the U.S. Government had excess local currency—Brazil, Burma, Ceylon, Egypt, Guinea, India, Israel, Pakistan, Poland, Tunisia, and Yugoslavia—but the number of such bilateral programs has since fallen to eight.

As of January, American funding commitments to the eight programs amounted to the equivalent of \$58,097,041. The eight countries were:

Egypt (\$7,500,127), India (\$9,019,093), Israel (\$43,869), Morocco (\$1,506,164), Pakistan (\$735,209), Poland (\$15,183,308), Tunisia (\$2,507,652), and Yugoslavia (\$21,601,619).

In the late 1960s, instead of using excess local currencies to finance the bilateral programs, the United States began granting long-term dollar credits to countries in which it had developed trade surpluses, and since then most new bilateral programs have been financed on that basis.

Phasing Out Old Programs

In the future, some of the excess-local-currency programs, such as the one with Israel, may be phased out, and others, such as the one with Poland, will probably be converted to dollar-credit financing.

In addition to the eight excess-local-currency countries, the United States now has bilateral arrangements with Argentina, Brazil, Burma, Guinea, Japan, Mexico, Rumania, Sri Lanka, and the U.S.S.R.

With some of these countries the United States has established joint co-operation commissions, a diplomatic tool favored by Secretary of State Henry Kissinger, and in such cases a unit of the commission, called the medical research working group, may provide a focus for the various projects in the bilateral program.

Détente gave birth to the bilateral programs with the U.S.S.R. and Rumania and strengthened that with Poland. The best known of the bilateral programs began to take shape in 1970, when Dr. Roger O. Egeberg, a special consultant on health matters to the President and Secretary of Health, Education, and Welfare, proposed such a program in Moscow to Dr. Boris V. Petrovsky, the Soviet Minister of Health.

Secret negotiations that lasted for more than a year resulted in an agreement that the two countries would join forces in cancer, heart disease, and environmental health research, and the agreement was made public in February, 1972. President Nixon and First Secretary Brezhnev signed it at their Moscow summit meeting three months later.

Except in the added area of schizophrenia research, where problems have arisen because of American reaction to the Soviet practice of hospitalizing political dissidents in psychiatric institutions, collaboration in health research between the two countries has since flowered.

Ehrlich's Office Focal Point

The focal point of the bilateral health programs here is H.E.W.'s Office of International Health, a 50-person unit headed by Dr. S. Paul Ehrlich in the Office of the Assistant Secretary for Health. Each of the six major agencies in the Public Health Service has at least three international affairs specialists to coordinate its own foreign programs. The largest of these major-agency staffs by far is the National Institutes of Health's Fogarty International Center, which coordinates N.I.H.'s many and varied research projects abroad.

EDITORIAL CAPSULES

... brief summaries of editorials or comments in current medical and scientific journals.

Stamp Out Food Faddism

"Food faddism is indeed a serious problem. But we have to recognize that the guru of food faddism is not Adelle Davis, but Betty Crocker. The true food faddists are not those who eat raw broccoli, wheat germ, and yogurt, but those who start the day on Breakfast Squares, gulp down bottle after bottle of soda pop, and snack on candy.

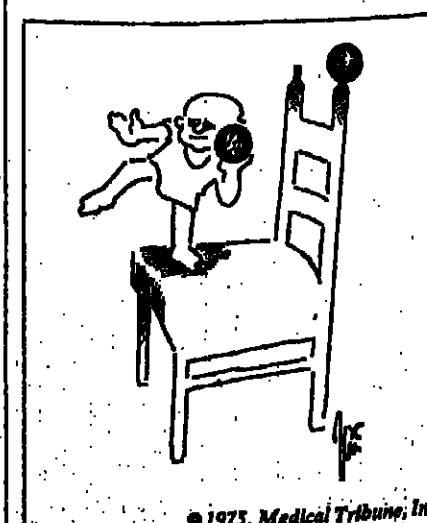
"Food faddism is promoted from birth. Sugar is a major ingredient in baby food desserts. Then come the artificially flavored and colored breakfast cereals loaded with sugar, followed by soda pop and hot dogs. Meat marbled with fat and alcoholic beverages dominate the diets of many middle-aged people. And, of course, white bread is standard fare throughout life.

"This diet—high in fat, sugar, cholesterol, and refined grains—is the prescription for illness; it can contribute to obesity, tooth decay, heart disease, intestinal cancer, and diabetes. And these diseases are, in fact, America's major health problems. So if any diet should be considered faddist, it is the standard one. Our far-out diet—almost 20 percent refined sugar and 45 percent fat—is new to human experience and foreign to all other animal life....

"It is incredible that people who eat a junk food diet constitute the norm, while individuals whose diets resemble those of our great-grandparents are labeled deviants...." (*Editorial, Nutrition Action, Mar.-Apr., quoted, Science, 188:714, May 16, 1975*).

Preventing Rh Disease

"All Rh-negative women who are at any risk of becoming sensitized to Rh must be protected with Rh immune globulin irrespective of whether they have had a term pregnancy, an abortion, or an accidental transfusion with Rh-positive blood. As stated elsewhere, it is the physician who, in the last analysis, will play a key part in the ultimate eradication of Rh disease. How quickly it disappears clinically depends entirely on how well the physician discharges his responsibility to the Rh-negative mother." (*Article, V.J. Freda, M.D., et al., N. Engl. J. M., 292:1014, May 8, 1975*).



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Nutrition

A Blackout for Medical Students...

MEDICINE CONFRONTS a disturbing dilemma. Linus Pauling, Roger J. Williams, Albert Szent-Gyorgi and other leaders have pointed to the failure of the "medical establishment" to undertake proper training of young doctors in the field of nutrition.

There has been an educational blackout in a key area of medicine—nutrition. Since the beginning of this century

a significant portion of the improvement of our general health, as it relates to physical status and longevity, is attributable to improved nutrition in large sectors of our population. Yet little is taught in nutrition even for such critical situations as pregnancy, diabetes, alcoholism and a wide range of metabolic disturbances, as well as surgical states.

... Blackout for Practicing Physicians

ADDED TO THIS DEFICIT, present regulations governing the sale of essential nutrients, such as lysine and other amino acids and vitamins, make it impermissible to send material to physicians which goes beyond the statement that preparations containing these elements are "nutritional supplements."

Thus the American medical profes-

sion suffers a double blackout—inadequate training in nutrition at medical school, virtually non-existent post-graduate nutritional education, and an interdiction of the use of published scientific reports by ethical pharmaceutical companies or others in printed material prepared for the medical profession.

What are Doctors and Patients "Learning"?

THE PRACTICING PHYSICIAN learns about most new therapeutic discoveries through published papers. These also attain added circulation when reprinted or exploited in promotion by pharmaceutical companies. On the other hand, nutrition is as rare in mass major professional medical periodicals as in the medical curricula. Most advances in nutrition are recorded in small, highly specialized journals of limited circulation. Articles on nutritional elements cannot be reproduced or distributed to physicians by producers of these substances. It is inconceivable that a section of the American therapeutic community, the manufacturers of vitamins or producers of vitamin preparations, are legally denied the right to send physicians a reprint of a scientific publication by Linus Pauling even if it was published in the *Proceed-*

ings of the National Academy of Science, or in *J.A.M.A.*, and that the same restriction holds if they were to mail chapters of a book on nutrition authored by Roger J. Williams and published by so prestigious a house as Charles C. Thomas. But that is exactly the case. On the other hand, there is no control either restricting or correcting inaccuracy or sensationalization of nutritional or dieting materials flooding the lay public.

Freedom of the public press is a precious thing and perhaps we have to pay a price in terms of health to protect against government censorship of science news. But how on earth does this jibe with forbidding the mailing to physicians of valid scientific reports by outstanding authors by organizations formulating prescription or non-prescription vitamins?

Needed:

Constructive—Not Destructive—Government Regulation

IT IS IRONIC THAT regulations ostensibly protecting the public serve to expose the "uninformed" to faddists and to unrestrained, unscientific speculation and unethical, commercial exploitation through shoddy preparations

and unscientific propaganda. And it becomes ridiculous that these same regulations impose a blackout on the distribution of scientific reprints to physicians who should be a source of informed guidance to patients. A.M.S.

The U.G.D.P. Fantasy Study of Diabetes

CLINICAL QUOTE: "No amount of statistical manipulation can compensate for the erroneous conclusions that are drawn from a study in which one-fourth to one-third of the patients did not have the disease under study, three-fourths of the patients should not have been given the drugs under study, the wrong dose of the drugs were used and the treated group had twice as much pre-existing cardiovascular disease as did the control group. The value of any therapeutic agent should be judged by the benefits that are obtained when it is used properly and not by the harm that results when it is used indiscriminately." (*Concluding paragraph of analysis of U.G.D.P. study by Dr. James M. Moss, Director, Georgetown University Hospital Diabetes Clinic, published in Medical Tribune, June 4, 1975*).



"Perhaps I'm nit-picking, Hippocrates, but 3,000 drachmas just for a consultation?"

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LETTERS TO TRIBUNE

Einstein, Planck, Pavlov

Your valued editorial on "Our Changed and Changing Era" prompts me to tell you of my interest in this and your other editorials. Most of the great scientists that I know of, e.g., Einstein, Planck, Pavlov, are very solidly against militarization. Pavlov, for example, says in his "Lectures on Conditioned Reflexes" (1928), which I translated:

"Let the mind rise from victory to victory over surrounding nature, let it conquer for human life and activity not only the surface of the earth but all that lies between the depth of the seas and the outer limits of the atmosphere, let it command for its service prodigious energy to flow from one part of the universe to the other, let it annihilate space for the transference of its thoughts—yet the same human creature, led by dark powers to wars and revolutions and their horrors, produces for itself incalculable material losses and inexpressible pain and reverts to bestial conditions." (page 41)

I look forward to reading your subsequent editorials on our "changed and changing era."

W. HORSLEY GANTT
Perry Point, Md.

Forcing Beliefs on Others

Dr. Sackler's column of Mar. 12, 1975 was very logically and rationally presented, and after reading the replies published on April 16, I wish to add my voice to those who support your position. I am absolutely dismayed to observe the lengths to which some people in our free society go to force their beliefs upon others who are not necessarily of like mind.

JOSEPH T. MORGAN, M.D., F.A.A.P.
Coos Bay, Ore.

Fetal Research Concerns

The total prohibition of all research that requires the use of fetal tissues is a source of concern for us all. Still, it would seem that the present impasse is more the result of intransigence on the part of those who demand total, unrestricted autonomy than any obstructive effort on the part of anti-abortionists.

While we all recognize the great humanitarian value of fetal research that is professionally and discretely conducted within broad boundaries of legitimate research, we must recognize too our ethical obligation to provide clearly defined, enforceable limits which proscribe indecent and abusive practice.

Only in this context, with guidelines clearly and effectively established, will responsible investigators be able to conduct much-needed experimentation free of fear or harassment.

RICHARD A. WATSON, M.D.
Brandenburg, Ky.

Riddle of Diabetes Mellitus

The final two sentences of the editorial, "Solving the Riddle of Diabetes Mellitus" (MT, April 16), read as follows: "The exciting and intriguing possibility is that failure to prevent microangiopathy and atherosclerosis in diabetics by insulin therapy may be turned to success with the addition of somatostatin to the therapeutic regimen. Time will tell."

May I point out that this statement, as far as I know, is not supported by any evidence nor even by a plausible hypothesis. What does the writer of this editorial know which is hidden from all others in the field?

I would not object so openly if it were only a matter of an unsupported statement. What I do object to is the effect such statements have on physicians and patients alike. They take it at face value and demand the wider use of such substances as somatostatin to "prevent angiopathy". It is ethically unconscionable to hold out such promises.

Somatostatin is a most interesting tool in endocrine research, but there is not the slightest bit of evidence relating its actions to blood vessels—small or large. It is cruel to hold out what may well be empty promises to diabetics in dread of advancing angiopathy. One perhaps expects such exaggerated deductions in the day press. A somewhat greater responsibility should be assumed by your journal.

RACHELLE LEVIN, M.D.
Duarte, Calif.

Single High Standard Urged To Reduce Infant Mortality

Continued from page 1

tality statistics are considered by the United Nations to reflect "at least 90 per cent of actual events," the U.S. ranks sixteenth—much poorer than Sweden (first), Japan, France, Australia, the United Kingdom, and Canada, he observed.

"Most of these countries have fewer physicians for the population and lower health expenditures than we do, so something other than socio-economic conditions and mere quantity of health services must be involved," commented Dr. Wegman, who is Dean Emeritus of the University of Michigan School of Public Health.

Shift in Priorities Asked

He recommended new efforts to equalize "the different needs for public health among various segments of the population," particularly blacks, and a shift in national priorities to achieve "the single high standard of health care for all the population which the National Commission on Community Health Services called for ten years ago.

"Why can't we seek the American goal of being number one in this, rather than in military expenditures?" he asked. "Infant mortality," he pointed out, "has been shown to correlate well with general health conditions and the state of the environment."

Dr. Wegman explained that the list of 25 countries eliminates one fourth of the world's countries with populations below the 2,500,000 mark, and another three-fifths of the remainder because of their unreliable statistics. The infant mortality rate for the listed countries is "the number of live-born infants who die before their first birthday, per 1,000 births," he added. In 1972, that rate was about 19 per 1,000 in the U.S., compared to 11 in Sweden.

A live birth, he said, is an infant who, after separation from the mother, shows at least one of the following signs of life, whether or not the umbilical cord is cut: respiration, heart beat, movement of voluntary muscle, or pulsation of the umbilical cord.

Japanese Progress Cited

To get around the problem of distinguishing live births and neonatal deaths from stillbirths, Dr. Wegman also compared the trend in mortality rates over a period of years. From 1955 to 1975, he said, "when the record for the United States was making disappointingly slow progress, the Japanese rate was maintaining a sharp and steady decline," despite its size, population density, and the harsh conditions of the post-war period. In addition, he said, from 1956 to 1971 the decline in first-week mortality in the U.S. was one-third, while in Japan it was two-thirds.

In a country like the Netherlands, where the rates even forty years ago were much lower than those in the U.S., "one might assume that the lower the absolute rate of infant mortality the more difficult would be further progress." However, Dr. Wegman showed

that the rate of decline in this country has been even more rapid than in the U.S. and is now less than Japan.

In a study of deaths after the first week of life, when the chief causes of death are more often preventable, the U.S. dropped from fourth place in 1956 to ninth in 1966, Dr. Wegman reported. This difference, like the others, could not be explained by differences in reporting alone, he added, and the lack of change in our relative position since then only demonstrates that, despite our improvements, "the other countries have improved at least as well, even though they were already lower than the U.S."

Dr. Wegman cited influences of genetic background, socio-economic status, and environmental conditions as possible causes for the poor status of the U.S., although, he said, "no one has yet shown any correlation between race, per se, and infant mortality."

Socio-economic conditions have been shown to influence infant mortality, he said, citing the "disturbingly constant" higher rates among U.S. blacks than the white population. But to eliminate blacks for the purposes of comparison "seems to me totally unacceptable and a denial of the responsibility any nation has for all its citizens," Dr. Wegman asserted.

Furthermore, if we do use only the U.S. white population, he said, "we

Queenan Stresses Accuracy In Determining Gestation Age

Continued from page 1

Gyn at the University of Louisville School of Medicine, said that there was a lot of room for improvement. The national rate of prematurity is 8 per cent, or 240,000 infants yearly, and of these Dr. Queenan estimated that at least 10 per cent, or 24,000, are delivered before term by induction of labor or Caesarean section, when the physician has failed to determine gestational age to within the crucial two weeks.

"This really is inexcusable in most cases," Dr. Queenan said, "considering the proven traditional and new sophisticated tools we have. It is especially unfortunate in view of the fact that as many as 25 per cent of all perinatal deaths are preventable, and undoubtedly some of this mortality is due to iatrogenic prematurity."

Reliable dating is also important in high-risk pregnancies, Dr. Queenan emphasized. When there is a question of delivering a preterm infant, so as to remove it from a relatively hostile environment, as in preclampsia, the physician must keep in mind that there is a great deal of difference between the extrauterine dangers and stresses to which an infant is exposed at 32 as opposed to 34 or 35 weeks of gestational age.

Thus, "we must not think that simply because we have got a positive LS ratio as determined by amniocentesis, in effect ruling out hyaline membrane



For a group of patients in Victoria, Australia, with cardiac arrhythmias, peace of mind is simply a telephone call away. Using an Australian-made electronic monitoring device, they receive daily checkups without having to move from their homes. Here, Dr. Tom Peter, of the Royal Melbourne Hospital, checks a heartbeat print-off while a technician demonstrates patient use of unit.

would be tenth in total infant mortality instead of sixteenth." Similarly, comparing the state of Minnesota alone, with its one per cent of blacks, to Sweden, the rate is indeed better than that for the entire U.S., but "still 70 per cent higher than the Swedish rate, not a very enviable status."

Dr. Shuman Backs Right of Prisoners To Psychosurgery

Medical Tribune Report

LAS VEGAS—Under some circumstances, a prisoner is entitled to a choice between psychosurgery which might remove the biological basis of his antisocial behavior and long term incarceration, Dr. Samuel I. Shuman told the 1975 National Medicolegal Symposium.

"If the relevant professional groups, acting through their professional societies, were to agree that an amygdalotomy for example, would significantly diminish abnormal aggressivity where there is a pathological brain site in the amygdala, and if a defendant with a history of conviction for aggression were to have such a brain site, I am not at all convinced that we should rule out the possibility that he be offered the alternative of the procedure or incarceration," said Dr. Shuman, Professor in the Law School and Department of Psychiatry at Wayne State University.

Consent Held Meaningful

Dr. Shuman disagreed with those who maintain that in the "coercive atmosphere" of the typical large prison the prisoner's "informed consent" to psychosurgery is essentially meaningless, a notion recently upheld in a Detroit psychosurgery case for which he acted as defense attorney.

"On the basis of my experience, I do not believe that prison makes all prisoners incompetent to make rational decisions about alternatives—even when they are so drastic as incarceration vs. brain manipulation. In a number of countries, comparable choices are offered convicted defendants. For example, chemical or surgical castration rather than imprisonment after a history of sex offenses," Dr. Shuman said.

'Innumerable' Cases of Patient Seduction 'Disgrace to Our Profession'—Masters

Continued from page 1

from the Tissue Committee comes along and says, 'Let's have a little chat.' However, "when we finish our formal education as psychotherapists, it is rare that we have any established review procedures outside basic hospital orientation. It is indeed rare that we have the privilege and the opportunity for our continuing education—namely, peer review."

In discussing some of the original concepts of sex therapy he conceived with Virginia Johnson, Dr. Masters reiterated his thesis that sex is not a learned phenomenon. "You know," he confided, "I used to be in obstetrics—a most absorbing, incredibly boring discipline, particularly at 3 a.m."

What Comes Naturally

To "relieve the tedium," he recalled, drawing guffaws from his listeners, "we would play a game—to see how many boy babies were born [in a given time] with erections. . . . The fact is that all baby boys erect and all baby girls lubricate within the first four to six hours of life" and, "obviously, there isn't time to learn how." It is sexual behavior that is learned, he stressed, not the capacity to respond.

Dr. Masters has said that roughly a quarter to a third of all couples' sexual dysfunctions "can and will be reversed if the authority has some basic knowledge of sexual physiology, of behavioral interaction, and simply is a very

willing listener." Only 3 or 4 per cent of sexual dysfunctions seen in his laboratory, he said, are metabolic in origin.

The blame for many, if not most, sexual dysfunctions he pins squarely on society's obsession with performance at the price of pleasure. "Fear of performance is usually the male's biggest problem," he stressed, adding that today's female is also feeling increasing pressure to perform.

Believing that "sex is a communication," eventually "a communication between two committed people," Dr. Masters' approach is to "treat the relationship and let mother nature take over the rest." He deals with dysfunction such as impotence by using sensate focus—the emphasis on pleasurable touching but not on genital stimulation or performance. Eventually, he affirmed, "performance takes care of itself."

Dr. Helen S. Kaplan, Clinical Associate Professor of Psychiatry, Cornell University College of Medicine, New York City, who chaired the session on sex therapy, commented: "Dr. Masters [with Virginia Johnson] has exploded the myth that sexual dysfunction is always part of a deep-seated problem."

Dr. Masters urged that physicians and other health-care professionals who treat dysfunctional couples take into account not only the overtly dysfunctional individual but the entire relationship.

One speaker who expanded on this theme was Dr. Clifford Sager, Clinical Professor of Psychiatry, New York's Mount Sinai School of Medicine, and Psychiatric Director of the city's Jewish Family Service. Most frequently, he has found, "sexual dysfunction . . . is so intimately connected with problems in communication . . . that treatment of the dysfunction alone will be of relatively little value in mending the overall fabric of the relationship."

Calling for cross-disciplinary cooperation between the marital therapist and the sex therapist, Dr. Sager likened the relationship to that which exists between surgeon and internist: "Both have learned many of the same principles, have experienced similar train-

Clinical Research Curbs Seen a Major Barrier to Schizophrenia Progress

Medical Tribune Report

WILLOW POINT, ALA.—"One of the greatest barriers to advances in schizophrenia, and indeed many disease entities, is the unnecessary limitations that seem to be collecting on clinical research," Dr. Ross Baldessarini, Associate Professor of Psychiatry at Harvard Medical School, told a symposium on schizophrenia, here.

"Though well-meaning, these restrictions are resulting ultimately in the discouragement of worthwhile attempts to develop new and improved forms of treatment," he said.

Commenting further on the matter, Seymour Kety, M.D., Professor of Psychiatry at Harvard, said it has become difficult to gain approval to try new drugs.

"No drug is completely harmless; every physician must take into consideration the benefit versus the risk potential," he pointed out.

Many of the most useful drugs, like digitalis or insulin, have definite risks which are overshadowed by their therapeutic value, he noted.

"Unfortunately, the pressures on our regulatory agencies are now such that we seem to require a new drug to be harmless," Dr. Kety said. "Perhaps it is this criterion which is responsible for the fact that new and important drugs are being developed and used more in other countries than in the U.S."

Chair Obeys Commands



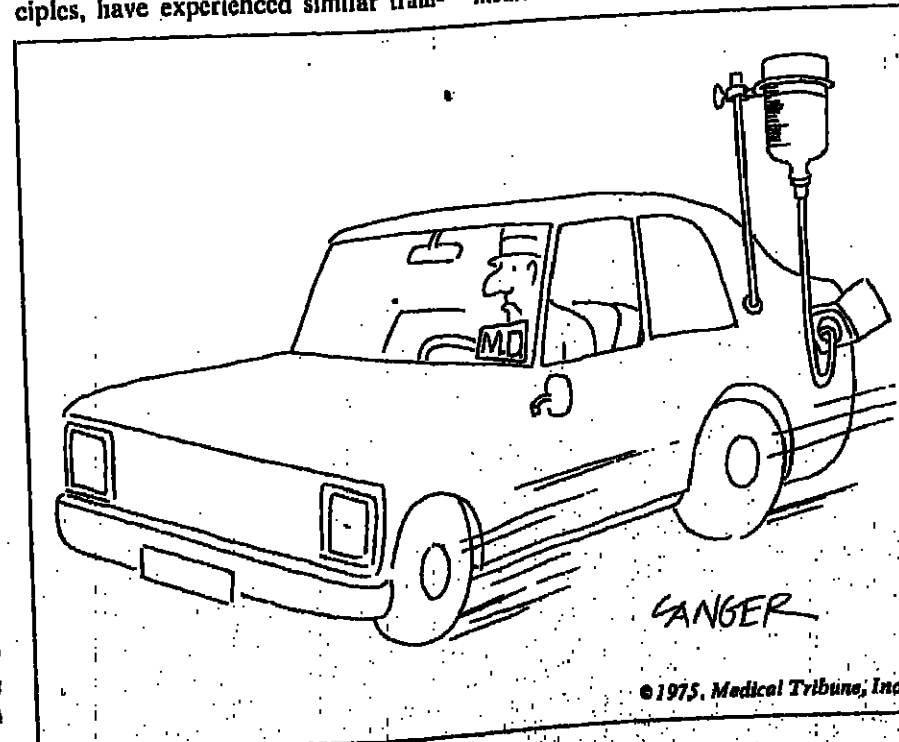
Engineers from N.A.S.A. have developed an experimental voice-controlled wheelchair (demonstrated by staff member). One feature is a robotic manipulator arm that can pick things up with two pincer fingers on command from the operator. The chair uses a miniature computer that accepts one-word commands.

ing in many areas. . . indeed, it is their knowledge and respect for each other's specialty that permits free flow of informed and responsible referrals."

'Return to Examining Table'

An old psychotherapeutic approach was suggested at an early-morning panel on sex therapy as it relates to psychiatric office practice by Dr. Alexander Levay of New York City, who said he trained with Dr. Masters and Virginia Johnson. Charging that many psychiatrists tend to be psychologically sophisticated, yet remote and medically frustrated, he offered a prescription: "Return to the examining table. It takes only 15 or 20 minutes to give a very thorough physical."

Should the psychiatrist feel "too rusty" to conduct an authentic physical examination, Dr. Levay suggests that he arrange at least to be present during the procedure. In so doing, "you gain more insight and understanding on a physical level; you also are greatly reinforced in initiating the therapeutic alliance of basic trust that you need." Many patients have sexual as well as other problems, he noted, "that are interfused between both psychiatry and medicine."



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New Data Back Insulin-Sensitive Sites Within CNS

Continued from page 1

a result of change in glucose utilization, the 2-deoxyglucose would block it and the insulin effect wouldn't be seen."

"The result," continued Dr. Andrew Szabo, "was that the insulin effect was identical in both the control animals—injected with buffer only and insulin—and in those pretreated with the 2-deoxyglucose. So we concluded that the insulin acts through another signal mechanism in the receptor cells, one that is not dependent on glucose utilization."

"What that other mechanism is, we don't know, but we tried to find where it is," he said. Therefore they designed experiments to see if the signal mechanism was in the sympathetic or the parasympathetic portion of the central nervous system.

They found that blocking either the alpha or the beta receptors of the sympathetic nervous system made no change in the insulin effect.

Cutting the vagus nerve, however, caused a partial inhibition of the response, said Dr. Andrew Szabo. And administration of the parasympathetic blocking agent atropine—given intraperitoneally—also caused a partial inhibition.

Cholinergic Nature Confirmed

"This was evidence that the regulatory mechanism is part of the parasympathetic nervous system. To localize it further, we injected atropine in small quantities into the carotid artery and this brought about a complete inhibition of insulin response. This suggested that either the receptor itself or the synapses of the neural route are cholinergic in nature."

The cholinergic nature of the system was confirmed, the investigators said, by pretreating the animals with neostigmine, a cholinesterase inhibitor. "By inhibiting cholinesterase," Dr. Olga Szabo explained, "we created an abundance of the neurotransmitter acetylcholine that released the atropine inhibition. In other words, we succeeded in inhibiting the inhibition."

Now, the team is trying to find where the neural regulatory system exerts its effects. They believe it acts at some step in the glycogen-manufacturing process of the liver. The hormonal glucoregulatory system appears to be separate from this, Dr. Olga Szabo added. "The hormonal system is slow, but of fairly prolonged duration. The neural system we are looking at, on the other hand is of short duration but very rapid."

Ibuprofen In Short Supply

Medical Tribune Report

KALAMAZOO, MICH.—The Upjohn Company is having difficulty in meeting heavier than anticipated demand for the antiarthritic agent ibuprofen. It says it will be late summer before significant improvement is seen in the supply situation, and has asked physicians to prescribe accordingly.

Leukemia Gains Widen Role For Practicing Pediatrician

By EDWARD GROSSMAN
Medical Tribune Staff

DENVER—Thanks to improvements in chemotherapy and treatment protocols, the practicing pediatrician may assume a larger role in caring for children with leukemia, Dr. John J. Hutter, Jr., associate director, Pediatric Oncology Center, Denver Childrens' Hospital, told a meeting of the American Academy of Pediatrics.

The major responsibility for treatment must continue to rest with tertiary multidisciplinary specialized centers, which alone have the expertise and resources to make accurate differential diagnoses and design the best treatment plan, Dr. Hutter said. But as rate and duration of remissions increase, and as intervals between hospital sessions of radiation as well as bone marrow and spinal fluid analysis lengthen, some childhood leukemias tend to become chronic rather than acute diseases.

As a result the family practitioner, especially in outlying areas, might be called upon to involve himself as follows:

Presenting Characteristics

• **Preliminary Diagnosis.** The physician should be aware of the presenting characteristics of childhood leukemia. Onset is usually between two and five years of age, and the majority of affected children are anemic. Over 70 per cent have platelet counts less than 100,000 and many patients have bleeding manifestations. There is usually evidence of adenopathy and hepatosplenomegaly.

• **Psychological support of young patients and their families.** Dr. Hutter emphasized the importance of the referring pediatrician's knowledge of the patient and his family, and of how they have reacted to previous stressful situations. This information is invaluable to the specialized team at the oncological center, and it is the basis for the physician's continuing support in the home and local setting. "We encourage the pediatrician to undertake this admittedly often difficult task," Dr. Hutter said.

• **Management of anti-leukemic therapy.** Studies show that patients receiving most of their regular care at the Denver Childrens' Hospital Pediatric Oncology Center, and those living far from Denver and relying on the family pediatrician to implement and monitor the treatment prescribed by the center, enjoy virtually identical patterns of remission.

All Achieve Remissions

Forty-two patients presented with acute lymphoblastic leukemia and were treated in 1969-1971. Twenty-seven lived close enough to Denver to receive all their therapy, and follow-up at the Center, while the remainder visited the Center only every three months, following initial treatment.

All children eventually achieved remissions, Dr. Hutter reported, after induction therapy with vincristine, prednisone, and cyclophosphamide,

and in four cases, Daunomycin. Maintenance chemotherapy for both groups consisted of oral 6MP, methotrexate and cyclophosphamide.

Follow-up and evaluation of the out-of-Denver group were performed by pediatricians in the patients' communities, who stayed in touch with the center by letter and telephone and could reach members of the oncology team on a 24-hour basis.

Of the 27 Denver patients, "three remain in continuous complete remission with a follow-up period of 50 to 70 months," Dr. Hutter said, "while of the 15 out-of-town patients, six remain in continuous complete remission after 48 to 65 months."

Later Study

In a later study, 37 children with acute lymphoblastic leukemia were seen and treated in 1971-1973. 34 received CNS therapy with 2400 R cranial x-ray plus 3 doses of IT MTX after complete remission had been obtained with vincristine, prednisone and cyclophosphamide. Maintenance drug therapy was the same as in the previous study, but rate of continuous complete remission was higher, both for the Denver and out-of-town patients:

Of 16 in the first group, nine had no relapses during a follow-up period up to 45 months; in the same period, 14 of 18 patients outside Denver and mainly being cared for by their pediatricians were also in uninterrupted complete remission.

The conclusion that Dr. Hutter drew was that some leukemic children "can be effectively managed within their own community by a practicing physician who has guidance and consultation available from a pediatric oncology referral center."

"We feel also that the improved overall continuous complete remission duration for patients on our second study is due to the specific CNS therapy of cranial radiation plus intrathecal methotrexate given early during remission."

Progress in Therapy

► In a related paper reviewing progress in cancer therapy, Dr. Alvin M. Maurer, Medical Director, St. Jude's Children's Research Hospital, Memphis, confirmed Dr. Hutter's experience that using combinations of intrathecal methotrexate and cranial irradiation, the incidence of CNS relapse in childhood lymphoblastic leukemia has been cut from 85 per cent ten years ago, to less than 10 per cent today.

In the same form of leukemia, control of concomitant bone marrow disease with multi-agent maintenance therapy has also been considerably enhanced, Dr. Maurer said, so that "in recent years half of the children have achieved at least five years of disease-free survival after diagnosis."

Problems remain, however, with that minority of patients with mediastinal masses and CNS disease at time of diagnosis; appropriate relapse protocols are yet to be designed for them, according to Dr. Maurer.

Teleprinter Linkage Enables Deaf to Use Phone



A first in the history of communications between the deaf recently took place when a deaf member of the British Parliament made a transatlantic telephone call to Dr. Boyce Williams (at keyboard) of H.E.W., who is also deaf. They communicated by means of an electronic device that allows the connection of two teleprinters by means of acoustic/inductive coupling to the standard telephone. This allows deaf persons to communicate with others over regular telephone systems by typing back and forth. Over 10,000 such units exist in the U.S., and fire and police stations are installing them so that the deaf may communicate in emergencies. Machines cost from about \$100 for a reconditioned model to \$750 for a new one. Couplers cost about \$135.

Some children with solid tumors also have a better prognosis due to recent chemotherapeutic, radiotherapeutic, and surgical advances, Dr. Maurer said. Patients with rhabdomyosarcoma may now undergo irradiation and chemotherapy to reduce the size of the tumor prior to surgery, thus pre-

serving the greatest amount of normal tissue and avoiding debilitation and disfigurement.

However, other varieties of tumors have remained resistant to any combined approach. Among these are neuroblastomas, for which survival statistics have not changed.

Acetaldehyde Is Implicated In Alcoholic Myocardiopathy

By HARRIET PAGE
Medical Tribune Staff

SAN FRANCISCO—Alcoholic myocardiopathy may result not from the direct effects of ethanol on the myocardium, but from the effects of its breakdown product, acetaldehyde.

Studies described here at the annual meeting of the American College of Physicians by Dr. Sidney S. Schreiber of New York indicate that acetaldehyde released from the liver may interfere with myocardial protein synthesis. Because this synthesis is quite rapid—every four to six days—repeated insults could result in the inefficient cardiac muscle that is typical of the condition, he added.

Perfused Guinea Pig Hearts

Dr. Schreiber, who is Professor of Medicine at New York University School of Medicine, performed the studies with Dr. Marcus A. Rothschild, also Professor of Medicine, and Murray Oratz, Ph.D., Associate Professor of Biochemistry at the N.Y.U. School of Dentistry, using isolated perfused guinea pig hearts.

"We know that alcohol exerts its damaging effects on the liver by interfering with its protein synthesis," Dr. Schreiber said, "so first we tried to find out if alcohol would have the same effect on myocardium." During three hours of perfusion, however, ethanol, 250 mg./100 ml., did not alter cardiac function or impair protein synthesis.

But when they repeated the experi-

ment with only 0.8 mM acetaldehyde, incorporation of radiolabeled lysine into protein decreased almost a half from the values seen with control and ethanol-perfused hearts. This occurred along with marked inotropic and chronotropic effects, Dr. Schreiber said.

"Next, we needed to find out if the decreased synthesis was the result of the overload effect—the faster, stronger beat—or occurred independently of it." In the next step they used the beta blocker propranolol to block these effects and this time found that protein synthesis—specifically of the microsomes—as measured by lysine uptake, was still inhibited.

The amount of acetaldehyde they used, Dr. Schreiber noted, corresponds to the levels seen in alcoholic patients. They next tried to localize the effects of the acetaldehyde. "In the liver, it destroys the ribosomes by destroying polysome aggregation. This wasn't the case with the myocardium."

Site of Synthesis Inhibition

By using an antibiotic that arrests the polysome pattern, however, they were able to find that the acetaldehyde inhibits synthesis at the level of the sarcoplasmic reticulum, he said.

"From these in vitro studies we are therefore speculating that myocardiopathy occurs as the result of the effects of acetaldehyde, released by the liver, on myocardial protein synthesis," Dr. Schreiber said.

One Man...and Medicine

ARTHUR M. SAGAL, M.D.
International Publisher, Medical Tribune



Is This How a Conscience Dies?

I DIDN'T SLEEP well that night. The day had started beautifully. Rosa brought me my usual breakfast. The coffee was delicious. The room was flooded with glorious sound—Cora had put on Brahms First, von Karajan conducting. The flowers were colorful and fragrant. I was leisurely reviewing the *New York Times* when Cora said, "The consulate is calling."

"The consulate?" I was baffled.

"Yes," she said.

I took the phone but couldn't recognize the name of the man calling although what he said was clear enough.

"There is a young doctor here whom you may be able to help. He is quite disturbed. His father faces death. He is relocating and may need some help in getting scientific papers published."

I can always find time for young doctors in trouble. "Send him over. By the way, what is his name?"

"August Stern."

The name rang a bell.

I asked my assistant, "Miriam, where have I heard that name before?" The file came out. I did have an extensive correspondence from American physicians regarding a "Dr. Victor Stern." The letters were appeals for intercession with the Soviet government in his behalf or editorial support to call the attention of American doctors to Dr. Stern's plight.

I had not acted on these requests. It has been the policy of MEDICAL TRIBUNE to meticulously avoid political issues, to devote itself to medicine, to the problems and principles of practice and research and, above all, to everything affecting patients.

I was uneasy. The coffee got cold; the newspaper uninteresting. I no longer noticed the flowers or heard the music.

I could never understand one thing in respect to the horror of the holocaust. How could it be possible that six million people could be gassed to death, put in ovens, and so few voices raised.

Where were the good Germans and the Poles, and so many of the French? I had always admired the action of the Danish king who, in protest, wore a yellow band with the star of David around his arm. Perhaps I never fully appreciated what that action meant. It was at Yad Vashem, the memorial in Jerusalem to six million dead, that I saw the names of the good Germans, the good French, the good Belgians, the priests, the ministers, and nuns, whose names were honored because they gave their lives for their fellowmen.

Judgment on them was easy, just as my condemnation of the others was easy.

Perhaps the latter was too easy.

I had been to Moscow on a WHO mission. At that time I was guest of the

Ministry of Health. I met some of their top officials, highly competent men who, if they were American, would probably be among our leading health administrators. I found that some of them were avid readers of MEDICAL TRIBUNE which they admired and regularly clipped. I met Russian psychiatrists, intelligent and capable, whose names I would see later in the press. My mission was discrete. It was limited to the establishment of a task force on world health manpower. My contacts and discussions during my Moscow visit focused exclusively on that subject. Two years later I was surprised by the cordial greeting of one of the top Soviet health officials when we chanced to meet at HEW offices in Washington. I was taken aback, finding it difficult to place the face when encountering it in the office of the top U.S. health official.

I wondered what the young doctor wanted. If it was related to the Stern case, what could I do? It had become a most uncomfortable day. And then I was informed, "Dr. Stern is here."

A wiry young man of medium height, gaunt of face, intense, speaking poor English. We both spoke slowly, he haltingly, but his message was painfully clear. He brought out clippings of his father's case. It pieced together the plea of a son's fight for his father's life, haunted by the realization that his and his brother's applications to leave the Soviet Union could be the cause of their father's death.

"Please help me save my father's life. He was sentenced to eight years in jail for bribery. They said he took gifts from patients for medical care and medicines. He is a good doctor and his patients loved him. They would bring him chickens, eggs, and other things like that. Bribery in Soviet law is only supposed to be with government officials. They disregarded that. They sentenced him to eight years. My father is sick. That sentence is death. Can you do something?"

The young man did not know that I knew a number of Soviet health officials or had other relationships that he could have asked that I use. He only knew that his father was to die and he was pleading for help to save his life.

"I'm sorry," I said. What a miserable phrase.

"As publisher and for all the years I have edited medical periodicals I have

made it a principle never to involve my personal beliefs or political and other interests in the scientific media with which I was involved."

What a cop out.

I wonder, did I really say that? Did I say, "It is a matter of principle."

What principle?

I was adamant, but shaken—and am still shaken.

Where were the good Germans and the good Poles? Where am I, the good American? What was it that Christ said, "Judge not, that ye be not judged?"

What happened to my memories, to the tears at Yad Vashem...?

"Maybe I can help you in another field. The consulate said you wanted some help in getting your papers published."

He was obviously disappointed. His tension mounted. He smoked cigarette after cigarette; his fingers and eyes were in constant motion. He gave me one of his papers. It was in Russian. I understood from what he had said that he was a psychologist but the paper contained mathematical equations.

"I am interested in relating mathematics to psychology and have published many papers. Can you help me publish a book?"

"A book?" I asked. "I don't know. I might be able to help you get some papers published."

"Why not a book?" he asked.

"Well," I opined, "I think this material is too new and I doubt a publisher would risk the cost of a book."

Now frank incredulity was superimposed on his prior disappointment. He asked, "Do you only publish books on old material in America?"

Good God, I thought, how can I be so insensitive and such a big idiot? I sat stupidly, unable to answer this most logical and simple question.

"Maybe I could help you publish an article," I ducked. "Let me call a friend who is a publisher."

I did.

"A book?" he said, "on stuff as new as that and the guy isn't even known?"

It was obvious my friend thought I had gone crazy.

"Maybe I can help him get an article published," he said.

I turned to the young man and said, "He also suggests you should have an article published until you are better known."

"How do you get better known here in America, with old stuff?"

I wondered what was going on inside his head. Apparently his scientific material had been published and he probably could have had a book on the subject published in the Soviet Union. But he had his principles. He wanted to leave Russia. He did leave and became an Israeli citizen. Now he was visiting the United States to help his father and to share his scientific findings. I sat there feeling more foolish by the minute. After an embarrassed pause, I suggested that when he had an article translated into English we would meet together with my publisher friend...

I received an address to which to send a letter of protest: Central Committee of Union of Medical Workers, Moscow, Leninski Prospekt 42, USSR. I haven't written. Principle?

Should I jeopardize the opportunity of scientific exchange with Soviet officials? Principle?

Should I change the policy, my policy and that of MEDICAL TRIBUNE? Principle?

Where were the good Germans, the good Poles? Where are the good Americans? Have you written yet to save the life of Dr. Victor Stern?

Is this how we compromise our principles and deaden our sensitivities? What counts more, one life or one principle?

Is this how we kill a conscience—how a conscience dies?

EPICRAMS—Clinical and Otherwise

There is no medicine to be found for a life which has fled.

Ibycus (c. 580 B.C.)
Fragment 23

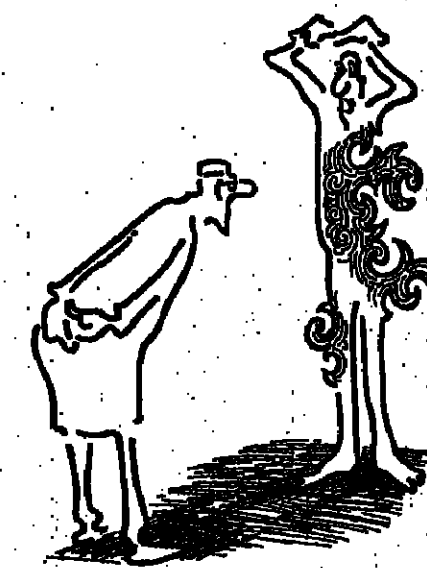
Medicine on Stamps

Nicolas Jose Gutierrez y Hernandez



Born in Cuba in 1800, he received his M.D. from the University of Havana. Becoming Professor of Anatomy, he published a manual on operative surgery. He later became chief surgeon of the Military Hospital, founded the Academy of Medical, Physical, and Natural Sciences in Havana and the Museum of Natural History, and started the first Cuban medical journal. After study in Paris he introduced in Cuba the stethoscope, the obstetrical forceps, plaster of Paris for fractures, chloroform, and many operations.

Text: Dr. Joseph Klar
Stamp: Minus Publications, Inc., New York



"Can you see any improvement?"
© 1975, Medical Tribune, Inc.

"Let me tell you about the medicine I'm going to prescribe."

TALKING OVER VALIUM®(diazepam) THERAPY WITH YOUR ANXIOUS PATIENT.



A patient often benefits by a greater understanding of his treatment program. You may find it helpful to make your patient aware that the purpose of therapy with Valium is to help reduce discomforting and disabling symptoms of excessive psychic tension and anxiety. It is beneficial for him to understand that much of his tension and anxiety can be relieved by your reassurance and counseling, and that these measures can do more than anything else to help him cope with his basic problems. The patient is reassured in knowing he can expect his medication to help him avoid feeling overwhelmed by his symptoms.

And it's also good for him to realize that he will be taking Valium only as long as he needs it.

Your expressed confidence in the medication prescribed, and the positive atmosphere in which therapy is given and accepted, work to the patient's advantage.

Selection of a dosage regimen is an important consideration when Valium (diazepam) is prescribed, and dosage should be individualized to achieve maximum beneficial effect. If the patient understands clearly when and how much to take, and if he knows why it's to his benefit to follow the regimen closely, the chances are better that he will take the medication precisely as directed. That should help avoid missed doses and discourage taking too much or too little medication — all of which can have an undesirable effect on the management of the patient's condition.

*"It's important that you
follow my directions
closely."*

*"I'll see you again the week
after next and we'll see
how you're making out."*

Your patient is often likely to feel reassured when you talk about seeing him again to check his progress. A planned visit evidences your continued interest and affords the patient an opportunity to report improvement he has made and to relate whatever continuing or additional difficulties he may be experiencing. It's also a chance for him to describe his response to therapy with Valium.

During follow-up visits, as your patient talks about his medication and about its effects on his symptoms, he will provide the kind of information that will be of great help in evaluating total therapy, adjusting the dosage of Valium, or discontinuing the medication entirely if that seems indicated.

Valium® (diazepam)

2-mg, 5-mg, 10-mg scored tablets
for individualized treatment of psychic tension



Please see the following page for a summary of product information.



Valium® (diazepam)

2-mg, 5-mg, 10-mg scored tablets

Prompt, effective action. Valium (diazepam) works rapidly to relieve pronounced psychic tension in patients overreacting to stress and in psychoneurotic patients.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other anti-

depressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Dosage flexibility. Scored Valium 2-, 5-, and 10-mg tablets give you dosage flexibility no tranquilizer capsule can match.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect. **Adults:** Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. **Geriatric or debilitated patients:** 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg—bottles of 100 and 500; Tel-E-Dose® packages of 100, available in trays of 4 reverse-numbered boxes of 25, and in boxes containing 10 strips of 10; Prescription Paks of 50, available singly and in trays of 10.



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110



A row of skulls with labels identifying injuries and unusual features was one of the most popular exhibits.

New York Times Photos

Treat for Mystery Buffs: Evening at the Morgue

MURDER INK, a bookstore on New York's Upper West Side, recently sponsored an evening at the morgue and a talk by Dr. Lowell J. Levine, a dentist who teaches forensic medicine at New York University, is a consultant to the Medical Examiner, and often travels 25,000 miles a year to testify on teeth. The invitations to the evening read, "Meet Me at the Morgue," and the exhibits included color photographs of cadavers, with comments by Dr. Levine. Speaking about unusual cases he has worked on, Dr. Levine said: "The only omnivores that can mimic human dentition are primates and the pig. . . I worked on a homicide where we considered the possibility that a pig had done it." After the lecture the mystery buffs moved to the morgue museum.



Some of the exhibits, including this mummified head, prompted Dr. Michael Baden, Deputy Chief Medical Examiner, to say to Mr. Lahary: "Watch the males. Females never faint; males faint."



Talking to guests are Dr. Levine (left) and Jean-Pierre Lahary (in striped shirt), curator of the morgue museum and a specialist in the reconstitution of cadavers. Mr. Lahary had just returned from work on the 346 victims of the Turkish DC-10 crash. "It's a special kind of work," said Mr. Lahary, who enjoys untroubled sleep. "You can do it or you can't."

Intrauterine Diagnosis Seen Taking on a Routine Aspect

By EDWARD GROSSMAN
Medical Tribune Staff

DENVER—Intrauterine diagnosis in the 2nd trimester of pregnancy to determine genetic and structural characteristics is fast becoming routine in certain cases. The object of these investigations, the fetus, may soon present as a possible patient for the clinician, Dr. Michael M. Kaback, Associate Professor, Department of Pediatrics, UCLA School of Medicine, told a joint meeting of the American Academy of Pediatrics, the American Pediatric Society, and the Society for Pediatric Research.

Among the various diagnostic procedures that have been developed, Dr. Kaback singled out amniocentesis as "an extraordinarily potent tool in the hands of the obstetrician, pediatrician, and medical geneticist." Assaying of amniotic fluid for fetal cells by surgical transabdominal perforation of the uterus is a procedure that is hardly ten years old, until recently considered experimental and hazardous. However, while a grand total of only 3,000 amniocenteses had been performed through 1973, an equal number were done last year alone, illustrating "exponential growth," Dr. Kaback said.

He attributed this increase to the greater confidence that physicians at genetic counseling centers have acquired as they have gained experience with the technique. Fifty-five of 80 centers in the U.S. and Canada now recommend and perform amniocentesis in some cases, with several of the centers accounting for as many as 150 procedures a year.

May Be 'Saturation Point'

That figure may represent a center's "saturation point," Dr. Kaback suggested, due to the limited number of trained personnel. He proposed that eventually all women over 35 who become pregnant be informed of the risk of giving birth to a child with chromosomal abnormalities, and be given the choice of undergoing amniocentesis, but he stated that "we have nowhere near the capability now to handle such a load." There are approximately 300,000 such pregnancies in the United States annually.

In every case in which amniocentesis is contemplated, the probable risk-benefit ratio must be weighed, Dr. Kaback said. At centers with experience, the complication rate from amniocentesis in the 2nd trimester is less than 1 per cent. Dr. Kaback emphasized that risks increase considerably in the 3rd trimester.

Women aged 35-39 with a family history of trisomy 21 (Down's Syndrome), but previously normal children run a risk of between 1 and 2 per cent of bearing a mongoloid child; in such cases the decision for or against amniocentesis is a matter of judgment. In women over 40 from such families, however, the indications in favor of amniocentesis are "clear-cut," Dr. Kaback said.

Women of any age who have borne chromosomally aberrant children should be seriously considered as candidates for amniocentesis. It has re-

cently been shown that women under 35 who have had a mongoloid child run a 1 per cent risk of recurrence, more than had been thought, Dr. Kaback reported. On the other hand, recurrence rates in trisomies 13-15 and 16-18 have not been established with any precision, therefore prior births in these categories do not by themselves justify amniocentesis. Likewise, Dr. Kaback advised against amniocentesis when the only indications are exposure to drugs or unusual levels of X-radiation.

For X-Linked Disorders

Amniocentesis is also useful, and is being increasingly employed, in the detection of X-linked disorders and inborn errors of metabolism.

A number of genetic diseases, principally hemophilia A and Duchenne muscular dystrophy, have no metabolic signs in the prenatal period.

Their probability may be tested for by determining the sex of the fetus. This is done by measuring the testosterone level in the amniotic fluid, or by karyotyping, which is now more than 99 per cent accurate, Dr. Kaback said.

Detection of inborn errors of metabolism by amniotic fluid cell culture is a burgeoning field, according to Dr. Kaback. "You have to keep up with the literature from week to week, it's expanding and changing so fast," he said. In the last five years, 25 errors have been successfully diagnosed *in utero*, and the criteria for diagnosis of another 40 have been agreed on, with the appropriate pregnancies to monitor being awaited.

Dr. Kaback cautioned that diagnosis of metabolic error is much more complicated than simple karyotyping. The literature includes two false positives for Tay-Sachs disease, in which the abortuses proved normal—these diagnoses were later shown to have been unreliable due to the fact that the amniotic cells had not been cultured. A high degree of expertise is also necessary to avoid misdiagnoses of enzyme deficiency diseases that are marked by crucially different levels of metabolic activity at various developmental stages pre- and postnatally. Moreover, the physician must distinguish enzyme levels in the heterozygous and homozygous fetus in order to prevent misinterpretation when dealing with autosomal recessive traits.

B-Scan Ultrasonography

A "most exciting new departure" in non-invasive intrauterine diagnosis is B-scan ultrasonography, Dr. Kaback went on. The fetal head, the placenta, spine and certain soft parts are being visualized with this modality, and most genetic counseling centers perform a B-scan routinely before amniocentesis, as ultra-sound measurement of head diameter is the most accurate method of determining gestational age in early pregnancy. Water-jacketed "gray-scale" ultrasonography has recently revealed fetal structures as fine as the inner ear and chambers of the heart at 14 weeks.

Finally, alluding to future developments, Dr. Kaback mentioned the promise of fetoscopy, which is in the

Faster Blood Flow



An improved arteriovenous shunt that allows blood flow in artificial kidney therapy to proceed three times faster than in standard equipment has been developed by University of Minnesota scientists. The short length and compact nature of the shunt provide reduced resistance to flow. Here, pointer indicates the connector between shunt outlet and dialyzer blood lines.

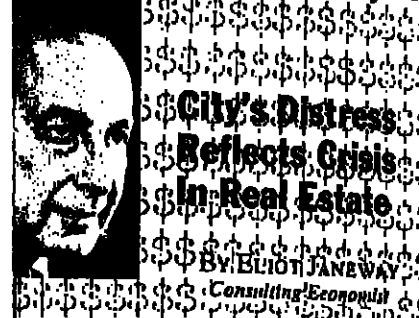
early stages of transformation from experimental to clinical technique. Fetoscopy allows direct visualization of the fetus by optical instruments. Such visualization would be of obvious value in obtaining samples of fetal skin and blood cells. Eventually, it could have application in inoculation and even surgery, as the fetus "becomes less an object, and more a patient."

In regard to fetoscopy as with ultrasonography and amniocentesis, Dr. Kaback expressed the hope that clinicians and investigators would always keep ethical considerations of diagnosis and therapy above considerations of mere technological innovation.



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Tribune Economic Analysis



City's Distress Reflects Crisis in Real Estate
BY ELLIOT JANOWAY
Consulting Economist

New York is more than just the biggest and sickest of America's cities. It is also a laboratory specimen of distress, revealing painful symptoms of spreading with the country's real-estate crisis.

The reason is that New York City's tax receivables are melting like snow in the heat of the sun. Landlords are using the proportion of rental incomes formerly taken by taxes to keep up with the jumps in their fuel bills. City Hall learned the hard way that it could not fight fuel costs or the utility costs rising in their wake.

The financing of new construction in the New York metropolitan market stopped a year ago. The financial lag has now caught up with tax foreclosures and tax assessments.

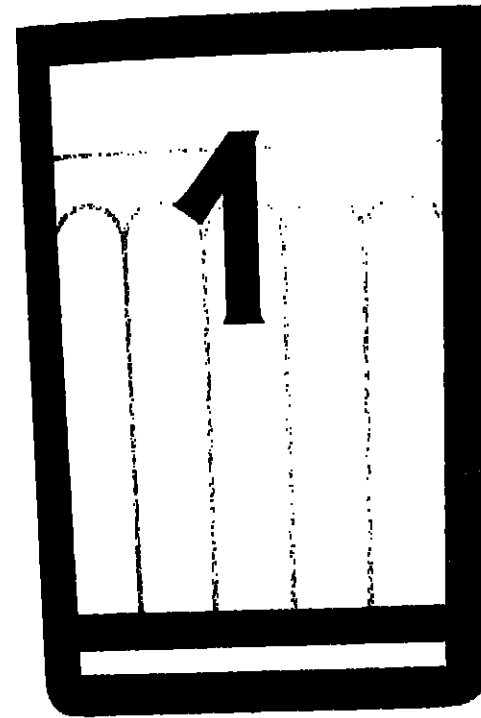
Taking over from landlords in arrears is no longer a problem for City Hall. Avoiding abandonments is. Slashing tax assessments as an incentive to real estate operators to hold or buy properties is too little, too late. Admittedly, New York City's real estate and related fiscal problems are horrendous. But they are by no means limited, and they could prove prophetic. Making generous allowance for the grotesque distortions and phony protection provided by New York City's crazy quilt of rent controls, a large and growing portion of New York property could not break even on operating costs before paying a nickel for taxes and interest, let alone mortgage-debt payoff. And that was before incomes started to shrink and rent collections to lag.

Pundits and policy-makers have been eyeing the length of the building slump and the sharpness of the drop in short-term interest rates as promising a recovery in building starts. They've been looking in the wrong direction. The sources of this slump are not domestic. They are traveling with the world oil-price gouge. If the federal government does not stop trying to borrow the economy out of this squeeze and does not start to bargain world oil prices down, the city governments dependent on their taxing powers to meet their payrolls and render public services will run out of credit.

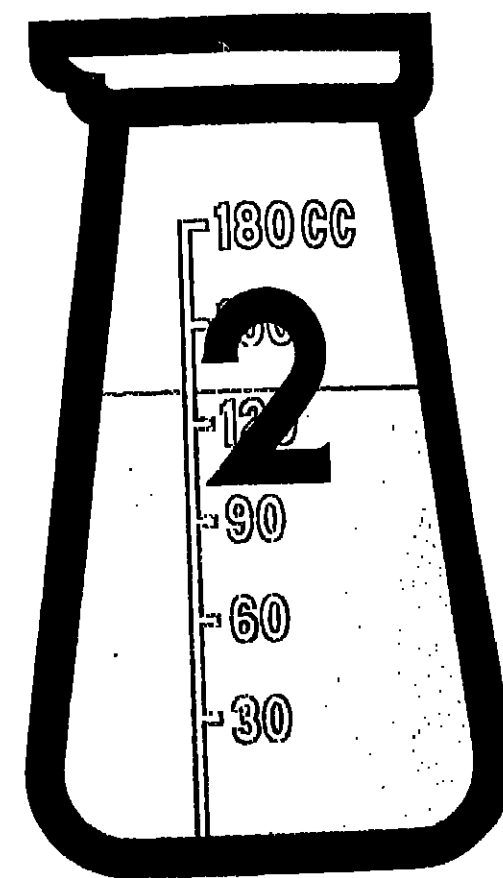
Talk with Janeway Yourself

The annual Janeway Seminar will be held at the Waldorf-Astoria, Park Avenue at 50th Street, New York, on June 19. Admission: \$250 for one participant; \$100 for each additional participant.

Among participants will be Jimmy Carter of Ga., Gov. Jim Egan of Neb., Senator Randolph of W. Va., N.Y. State Sen. Stanley Steingut.



Adequate fluid intake



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• Effective against susceptible *E. coli*, *Klebsiella*, *Aerobacter*, *Staph. aureus*, *Proteus mirabilis*, and, less frequently, *Proteus vulgaris*

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Acute, recurrent or chronic nonobstructed urinary tract infections (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms.

Note: Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides, especially in chronic or recurrent urinary tract infections. Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

Contraindications: Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A beta-hemolytic streptococcal infections and will not eradicate or prevent sequelae (rheumatic fever, glomerulonephritis) of such infections. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical

signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy. Insufficient data on children under six with chronic renal disease.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma, in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: Blood dyscrasias (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); allergic reactions (erythema multiforme, skin eruptions, epidermal necrolysis, anaphylactic shock, pruritus, exfoliative dermatitis, conjunctivitis, photodermatitis, periorbital edema, arthralgia and allergic scleritis); gastrointestinal reactions (nausea, vomiting, abdominal pain, hepatitis, diarrhea, anorexia, pancreatitis, stomatitis); CNS reactions (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); miscellaneous reactions (drug fever, chills, toxic nephrosis with oliguria and anuria, pericarditis nodosa and L.E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diabetes and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis).

Usual adult dosage: 2 Gm (4 tabs or teasp.) initially, then 1 Gm b.i.d. or t.i.d., depending on severity of infection.

Usual child's dosage: 0.5 Gm (1 tab or teasp.)/20 lbs of body weight initially, then 0.25 Gm/20 lbs b.i.d. Maximum dose should not exceed 75 mg/kg/24 hrs.

Supplied: Tablets, 0.5 Gm sulfamethoxazole; Suspension, 0.5 Gm sulfamethoxazole/teaspoonful.

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Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

What's In A Word?...

Continued from page 5

deal more detail, and the specific rewards, punishments, or deprivations are applied in a much more systematic and regular manner. Over time, the theory underlying such programs and the permutations with which they can be administered have grown more com-

"...I suspect that good rehabilitation programs are called *rehabilitation* and bad ones are called *behavior modification*..."

plex. For example, it is common in behavior modification programs dealing with the suppression of addictions to encourage new alternative behaviors as well as discouraging the addictive behavior which is to be extinguished.

At its simplest level a behavior modification program for profoundly retarded incontinent adults on a ward in a state school for the retarded might well reward patients with candy every time they used the toilet appropriately. At a more elaborate level, institutionalized juvenile delinquents might receive cash reward or special privileges for completing school assignments, taking responsibility for keeping their own quarters neat or for refraining from combative or assaultive behavior.

Behavior Therapy for Phobias

A form of psychotherapy based on the same general principles is more commonly called behavior therapy than behavior modification but the methods used bear some similarity. For ex-

ample, a patient with phobias about heights or crowds is desensitized in fantasy to these fears in a systematic progressive and careful manner. The patient is taught how to relax and then is gradually brought to tolerate larger and larger doses of the kinds of situations or phenomena he or she fears.

Another form of behavior therapy that raises more of the issues commonly associated with behavior modification is the approach known as "flooding." In it a patient, for example a severe obsessive, compulsive patient with an almost delusional fear of dirt and germs and a strong need to wash his hands every few minutes, is, with his initial concurrence, forcibly prevented from washing his hands for a prolonged period while being forced to face the kinds of dirt and germs he fears.

This treatment has been clearly

shown to substantially reduce obsessive compulsive symptoms for a prolonged period. The intense painful exposure to the things a patient fears most, though unpleasant, turns out to be substantially beneficial. Patients with anorexia nervosa—a pathological avoidance of eating—have been treated by behavioral principles on psychiatric wards. The general approach has been to make access to things the patient strongly desires contingent upon the

"Parental love and approval is often given to reward children for good behavior, and parental disapproval or even physical punishment is often given to suppress undesirable behavior..."

eating of a certain amount of food. Patients who might well continue to lose weight and have been known to go on to die under conventional psychotherapeutic and psychiatric ward management approaches (including even tube-feeding) can have their condition strikingly improved by the use of behavioral principles.

The issue then is not whether behavior modification is bad but whether it works.

Next week Dr. Cole will discuss applications of behavior modification to bedwetting, its proper use in prison, the deprivation of patients' opportunities by the irrational banning behavior modification and the use of psychotropic drugs.

Rising Uranium Demand Seen Miner Health Peril

Medical Tribune World Service

BORDEAUX, FRANCE—World demand for uranium is expected to climb to some 60,000 metric tons by 1980, as more countries turn to nuclear power as an alternative to oil. The figure will double again by 1985, and will bring with it increasing risks to uranium miners and millers, according to Dr. Ernest Mastromatteo, chief of the International Labor Organization's occupational safety and health branch.

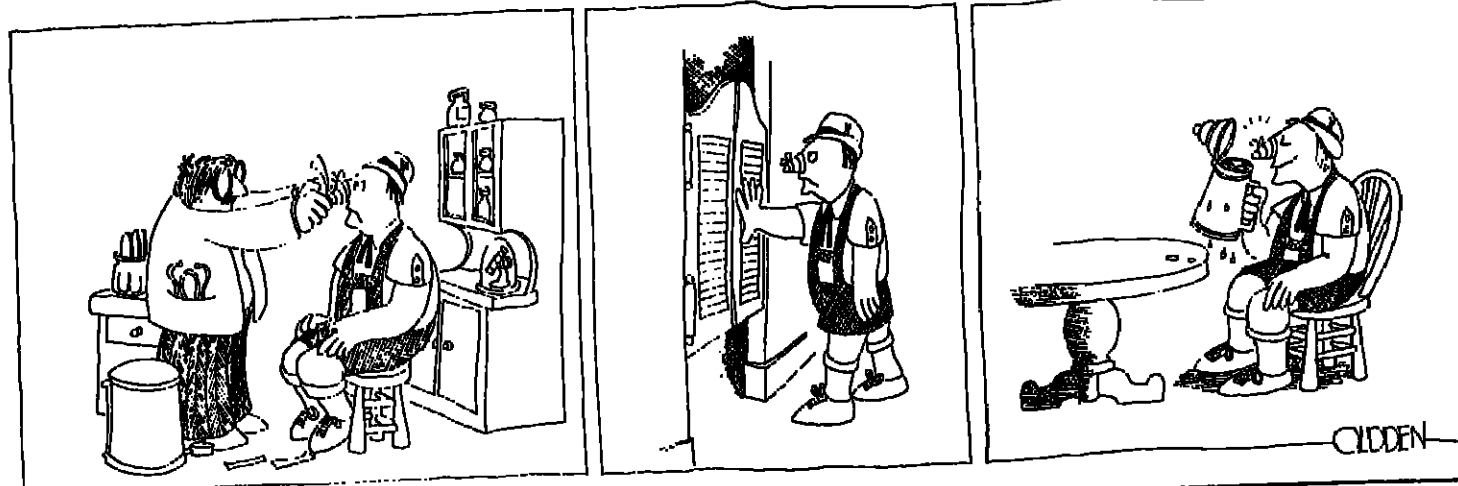
In spite of the progress made in recent years in radiation protection, the death rate among uranium workers remains alarming, he told an international symposium here on radiation protection in uranium extraction and processing.

The main hazard Dr. Mastromatteo noted, is radon, which diffuses into the working environment, where it decays into radioisotopes of polonium, bismuth, and lead. These radon daughters attach themselves to dust particles and, when inhaled, can lead to cancer of the lung.

The risk was demonstrated in a paper by Dr. John Muller and William Wheeler, of the community health standards division of the Canadian Ministry of Health. They said that among 8,649 past and present Ontario uranium miners, 75 of 368 deaths from 1955 to 1972 were due to malignant neoplasms, including 41 tumors of the lung.

In both the 45-49 and 55-59 age groups, pulmonary carcinoma deaths were about five times the statistical average.

Clinical Trials



TRIBUNE SPORTS REPORT

Athletes Advised to Develop Agility in Dodging Doctors

Medical Tribune Report

SAN FRANCISCO—Two doctors have offered some unusual advice to athletes: "Avoid doctors."

Otherwise, said Dr. George A. Sheehan, the running physician from Red Bank, N.J., and Dr. Joan W. Ulyot, director of the Aerobics and Physiology Division at the Institute for Health Research here, an athlete can lose his insurance, be taken out of training at the risk of losing his job, or end up in the coronary care unit of the nearest hospital.

Routine Abnormalities

They reported, in separate presentations here, on a number of so-called abnormal physiological and metabolic findings routinely detected in highly trained athletes.

Dr. Sheehan asserted that "doctors don't know how to treat athletes because they don't know what to make of what they find."

Many athletes will have an abnormal ECG—hypertrophic, hypertrophic, showing a rhythm disturbance, or a repolarization anomaly, he said. This last problem benched basketball player Dave Stallworth and would have done the same to Wilt Chamberlain if his physician had been a cardiologist, Dr. Sheehan added. He also gave these examples:

- Studies of distance runners at the Rome Olympics showed 80 per cent with abnormal ECGs.

- Two members of the Phoenix Suns had such abnormal ECGs that they were referred for cardiac catheterization.

- ECG studies of the 1972 New York Giants disclosed that four were hypertrophic, 50 per cent hypertrophic, one had a rhythm disturbance, and one out of six a repolarization anomaly. One was sent to the Mayo Clinic for further testing but proved normal, and the ECG of another player who had undergone knee surgery and did not train for a while returned to almost normal.

"No one who knows anything about ECG patterns would have read these as normal, but would have taken a player out of uniform and sent him to a hospital," Dr. Sheehan commented.

"We don't know why this happens, but we can't inflict our ignorance on athletes. Any physician who takes an ECG on a highly trained athlete should think, 'No matter how abnormal this looks, I think this man is in great shape and I'm learning something.'"

"The only danger in an athletic heart is going to a doctor."

Dr. Ulyot, who directs a portion of a long-range study to determine just what normal health is, declared that the medical profession "has no idea of normality or health because all 'normality' is based on sick people."

Several thousand subjects, many of them athletes, are participating in the study, which has documented misleading abnormalities in the resting pulse and certain enzyme levels in athletes, as well as the ECG abnormalities, she said.

Despite the fact that 70 to 90 is considered a normal pulse rate, "in runners we have yet to find one over 60 and more likely they are in the 40s," Dr. Ulyot reported.

"A good long-distance runner should wear a dog tag that says his pulse is 30 to 40 and that his ECG is bizarre," she suggested. "Otherwise, if he is sent to the hospital for any reason, he will end up in a coronary care unit."

Also, while elevations of SGOT, transaminase, and LDH levels are considered signs of a heart attack, in runners who average 80 miles a week the levels of these enzymes are nearly double the so-called normal, she said, and provide "further evidence that something drastic has happened."

Unnecessary Hospitalization

Dr. Ulyot related that these abnormalities were found in a top distance runner during a physical examination and that he was hospitalized for three weeks before she heard about it and told his doctor that "all runners have these abnormalities."

Other runners have been cautioned after checkups that they are "very sick" and must stop training, because of the danger of a heart attack at any time, she said.

The Institute for Health Research studies have disclosed several other metabolic differences between runners

Aid to Drought Victims



Red Cross aid to drought victims in West Africa includes a medical care and nutrition program. The main target is the child under 10, who often comes last in the order of priority in a family on the edge of starvation. Here, an emaciated girl has her first bowl of fish-meat porridge brought by a Red Cross team.

and nonrunners, Dr. Ulyot continued. Fit distance runners for example, have triglyceride levels of 56 to 60, considerably lower and in a much narrower range than the 80 to 140 typically found in the untrained individual, she said.

"The lazy man's way to fitness will not affect the triglyceride levels," she noted. "Exercise must be aerobic, strenuous, and at least every other day."

The untrained and the trained also utilize different types of energy, she said. The untrained person on a treadmill burns 60 per cent fat and 40 per cent glycogen, whereas the long-distance runner, working at 80 per cent of capacity, burns 90 per cent fat and 10 per cent glycogen—a finding that emphasizes the role of training, not diet, in athletics, she remarked.

The symposium was cosponsored by the American Academy of Podiatric Sports Medicine and the California College of Podiatric Medicine.

IMMATERIA MEDICA

Shaping Up in Arizona

"...while the fracture between its surgery department and the Arizona Medical Center has been splintered..."

So said *Medical World News*. To Dr. Gordon M. Meade, of the University of Rochester Medical Center, it sounded "as though things may be mending but they're still bent and out of shape."

You Can Call Me George...

Not long ago we read in the *New York Times* of the engagement of Princess Christina of The Netherlands and Jorge Guillermo and how it was press-released at the residence of the Dutch Consul General in New York. Mr. Guillermo came to the United States in 1960 from Cuba with his father, a physician, and his mother, an educational expert.

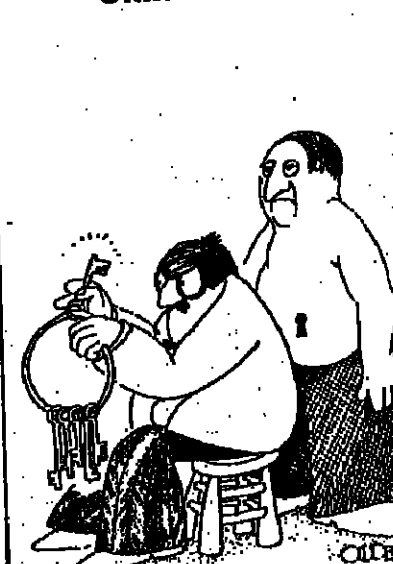
Anyway, the Princess, who is giving up her right to succession by marrying Mr. Guillermo, was asked by reporters when she first met her fiancé.

"I first knew Mr. Guillermo..." she began.

"Oh, you can call me George," he said. She burst into laughter with him and laid her head on his shoulder.

So the next time your wife calls you "Doctor," just say: "Oh, you can call me George..." and see if she laughs.

Clinical Cliché



Locked bowels.
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